ONCB JOURNAL

OFFICE OF THE NARCOTICS CONTROL BOARD, MINISTRY OF JUSTICE

Volume 40, Issue 2 (April - September 2024)

ONCB

- Thailand's Alternative Development Model towards the United Nations Guiding Principles on Alternative Development (UNGPs on AD)
- Drug User Poplation : Findings from the 2024 Thailand National Household Survey
- Heroin Epidemic Situation Among Juveniles
- Discovering the Problems and Identifying Preventive Solutions for Heroin Use Among Children and Youth in the Western Region of Thailand
- Acute and Chronic Toxicity Studies of the Standardized Kratom Leaves Aqueous Extract in Sprague-Dawley Rats

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ONCB

Vision

"To be a focal agency in coordinating narcotics control cooperation of the country and at international level in order to enhance social safety and humanity security."

Mission

(1) To determine the national policies and plans on narcotics control, as well as administer and supervise the execution by relevant government agencies and partner organizations

(2) To study and analyze problem situation, support technical information, and disseminate knowledge and understandings about drugs to the public

(3) To coordinate international cooperation on narcotics control

(4) To issue regulations and administer the enforcement of drug-related laws and other related laws effectively

(5) To perform duties and enforce drug-related laws as assigned

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Objectives

The ONCB Journal is an academic journal on narcotics. It aims to be a medium of dissemination and exchange of narcotics control information among scholars, practitioners, and the general public. In addition, it is also intended to facilitate the collaboration and implementation concerning narcotics control as well as encouraging public involvement in illicit drug monitoring and control.

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Editorial

The Office of the Narcotics Control Board (ONCB) remains committed to promoting and disseminating knowledge as well as serving as a platform for sharing technical evidence and research on drug-related issues. This 40th year edition of the ONCB Journal, Issue No. 2 (April-September 2024), features a selection of insightful and beneficial articles chosen by the editorial team. These include: 1) Thailand's Alternative Development Model towards the United Nations Guiding Principles on Alternative Development (UNGPs on AD), 2) Drug User Population : Findings from the 2024 Thailand National Household Survey, 3) Heroin Epidemic Situation Among Juveniles, 4) Discovering the Problems and Identifying Preventive Solutions for Heroin Use Among Children and Youth in the Western Region of Thailand, and 5) Acute and Chronic Toxicity Studies of the Standardized Kratom Leaves Aqueous Extract in Sprague-Dawley Rats. Those interested in studying or developing body of knowledge on drugs can access, search, or download the articles via the ONCB website (https://www.oncb.go.th) and the Narcotics Control Technology Center (NCTC) website (https://nctc.oncb.go.th). Additionally, you can become part of the ONCB Journal by submitting academic articles or research on drug-related issues to us. For more details or further inquiries, please contact the ONCB Journal editorial team.

The editorial team sincerely hopes that this edition of the ONCB Journal will be an inspiration for the development of knowledge, the dissemination of academic works to practitioners both domestically and internationally, and the contribution to appropriate responses to drugs. Should you have any comments or suggestions, we, the editorial team, are pleased to welcome them to continue improving the ONCB Journal. Lastly, the editorial team would like to express our gratitude to all researchers and authors for their articles given, as well as all readers for their interest and continued support of the ONCB Journal.

(Mr. Suvit Tharitkul)
Executive Editor and Publisher

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Thailand's Alternative Development Model towards the United Nations Guiding Principles on Alternative Development (UNGPs on AD)

| Ms. Rachanikorn Sarasiri*
Advisor to the ONCB

Thailand has long played a significant role in addressing the drug problem through alternative development at the international level. Alternative development is the development upon a participatory approach that involves the active participation of opium poppy growers, which is a crucial factor in addressing opium poppy cultivation. This approach requires the cooperation of opium poppy growers to cease growing opium poppy for income and instead cultivate other legal cash crops as substitutes. Moreover, these farmers are supported in various aspects of development to improve their livelihood, enabling them to find alternative ways to earn their living with a sustainable income and good profit. This is to motivate them to change their attitudes and behaviors towards opium poppy cultivation. Thailand's alternative development efforts stem from the royal initiative of His Majesty King Bhumibol Adulyadej The Great when His Majesty created the Royal Project in 1969. This initiative aimed at addressing the problem of opium poppy cultivation by the Thai hill tribes, which involved slash-and-burn practices that caused deforestation and environmental degradation. The Royal Project served as a prototype for alternative development projects, focusing on reducing opium poppy cultivation areas while improving the quality of life for the Thai hill tribes. Later in 1992, His Majesty King Bhumibol Adulyadej The Great demonstrated his royal vision to change the status of the Royal Project to be registered as the Royal Project Foundation under Royal Patronage. This change established the foundation as legal entity and a non-profit public organization, ensuring its sustainable operation. In addition, Thailand's alternative development initiatives were further inspired by Her Royal Highness Princess Srinagarindra, the late Princess Mother. Motivated by His Majesty King Bhumibol Adulyadej The Great's vision, Her Royal Highness initiated the Doi Tung Development Project in 1988. This project aimed at restoring degraded areas and the environment to their original conditions, improving the quality of life of the Thai hilltribes in the Doi Tung area, and addressing the severity of the illicit drug problem in the area. The Doi Tung Development Project is managed by the Mae Fah Luang Foundation under Royal Patronage. At present, His Majesty King Maha Vajiralongkorn Phra Vajiraklaochaoyuhua (King Rama X) has made firm commitments to nurture, conserve and extend the work of the Royal

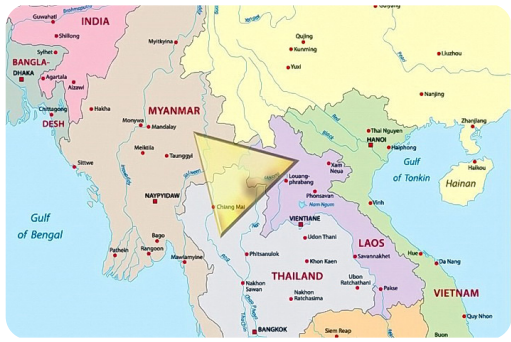
* Ms. Rachanikorn Sarasiri, Deputy Secretary-General of the Narcotics Control Board (2014 - 2015).

Project and the Royal Project Foundation under Royal Patronage. This dedication ensures the continued operation and sustainability of these initiatives, honoring the vision of of His Majesty King Bhumibol Adulyadej The Great. King Rama X is the Honorary President of the Royal Project Foundation. During his reign, the Ler Tor Royal Project Development Centre was established as the first Royal Project Development Centre and was designated as the 39th Royal Project Development Centre, dedicated to the remembrance of the late His Majesty King Bhumibol Adulyadej The Great.

Thailand was successful in implementing the alternative development to solve the problem of opium poppy cultivation. This led to the continuous reduction in opium poppy cultivation area, and Thailand was removed from the list of countries producing opium. In 2022, Thailand had only 106.25 rai (17 hectares) of opium poppy cultivation, after which the United Nations declared Thailand opium poppy cultivation-free. The United Nations adopted Thailand's alternative development model as a prototype for implementing the alternative development efforts as early as the 1950s. On 12 December 1994, Mr. Giorgio Giacomelli, Executive Director of United Nations Drug Control Programme (UNDCP), was granted an audience to present a gold medal award to His Majesty King Bhumibol Adulyadej The Great, recognizing His Majesty's valuable contributions to solving the drug problem. The United Nations had provided assistance to Thailand in addressing opium poppy cultivation since 1971, taking His Majesty's initiatives on crop replacement and alternative development as a model for implementation in Thailand and other countries facing the problem of narcotic crops cultivation. Thailand had since shared its experiences and knowledge in alternative development with other countries.

Opium Poppy Cultivation in Thailand

Over the past 100 years, narcotic drugs, which were widely spread and heavily abused, primarily originated from narcotic plants such as opium. Opium abuse evolved as it was processed into heroin by international illicit drug trafficking groups seeking sources of illicit opium to use as raw material for heroin production. This phenomenon led to the widespread production, trafficking, and abuse of large quantities of heroin. One of the world's most significant opium poppy cultivation area is the Golden Triangle, spanning approximately 200,000 square kilometres and overlapping the borders of three countries, namely northeastern Shan State in Myanmar, eight northern provinces in Thailand, and seven northern provinces in Lao PDR. Opium is classified as a narcotic drug under Category I of the Single Convention on Narcotic Drugs, 1961, as amended by the 1972 Protocol, and is also controlled under Category V of the Narcotics Code, 2021 of Thailand.



The Golden Triangle

Opium Poppy Field

In Thailand, opium poppy cultivation is carried out in the highlands of eight northern provinces by Thai hill tribes, including Chiang Mai, Chiang Rai, Tak, Phayao, Mae Hong Son, Lampang, Kamphaeng Phet and Nan. The hill tribes use opium for curing deceases, traditional ceremonies, trade, and personal consumption. Opium plays a significant role in the lives of Thai hill tribe, and illicit opium trade persisted for a long time. Opium is deeply intertwined with the way of life of the hill tribes, who are often impoverished, as opium poppy serves as their primary cash crop. During 1955 - 1956, it was estimated that 200,000 hill tribe farmers, including the Hmong, Yao, Lahu, Akha, Karen and Hor, cultivated opium poppy, producing an annual yield of approximately metric tons. Tracing back to the 1960s, large-scale opium poppy cultivation tool place in the Golden Triangle, particularly in Myanmar, which became the second-largest opium poppy grower after Afghanistan. Thailand also experienced significant opium poppy cultivation during this period, which led to environmental degradation due to slash-and-burn cultivation practices and deforestation caused by hill tribes clearing highland areas for opium poppy farming. International illicit drug traffickers purchased opium to process it into heroin in the Golden Triangle, perpetuating the illicit opium trade as a means of livelihood. Opium poppy cultivation became a serious problem for Thailand at that time. By 1965, the opium poppy cultivation area in Thailand covered 17,920 hectares, or 112,000 rai (6.25 rai = 1 hectare).

Prototype of Alternative Development Model

In accordance with the vision and far-sightedness of His Majesty King Bhumibol Adulyadej The Great, the solution to opium poppy cultivation was initiated during the 1960s. This effort began after His Majesty had visited the people in remote northern areas since 1964 and observed that Thai hill tribes were impoverished, earning their living by growing opium poppy for sale and cutting down trees in the forest for opium poppy cultivation. His Majesty sought to improve the living conditions of these hill tribes and thus introduced the concept of crop replacement to address the problem by promoting other temperate cash crops that provide incomes comparable to those from opium poppy. In 1969, His Majesty King Bhumibol Adulyadej The Great initiated the Royal Project, aiming to reduce opium poppy cultivation, improve the quality of life for hill tribes, and rehabilitate forest and water resources. Over time, His Majesty recognized that crop replacement alone was insuffucient.

Integrated development in other areas - such as public health, infrastructure, education, transportation - was necessary and should be brought in. This broader approach led to the emergence of the term alternative development. The Royal Project bacame the prototype for Thailand's alternative development model, combinding crop replacement programmes with integrated development to enhance the living conditions of Thai hill tribes. This model enabled the hill tribes, who once relied on opium poppy cultivation, to transition to cultivating other cash crops that provided better income and improved their overall quality of life. The World Drug Report of 2015 mentioned that Thailand's alternative development efforts have evolved since His Majesty initiated the Royal Project in 1969. Over the past 55 years, the Royal Project has successfully reduced opium poppy cultivation areas, alleviated poverty among hill tribes, and preserved highland environments from destruction caused by opium poppy farming. In 1988, the Royal Project was awarded the Ramon Magsaysay Award in recognition for the international understanding, and later in 2003, it was recognized as an Outstanding Organization for Efforts to Combat Drug Problems in Asia-Pacific Region by the Drug Advisory Programme of the Colombo Plan Secretariat.

The evolution of the Royal Project was marked in 1992 when it transitioned into the Royal Project Foundation under Royal Patronage, which aimed to align with the implementation of the Royal Project and to ensure its stability. The Royal Project focused on researching plant species to identify cash crops that could be promoted for farmers to grow as a source of, alongside integrated development initiatives. His Majesty King Bhumibol Adulyadej The Great's royal visits to the highlands and remote areas where Thai hill tribes lived enabled him to observe their living conditions and the various problems they faced. These observations guided the Royal Project in alleviating suffering and solving problems in ways that were appropriate to the race, culture, social context and environment of the hill tribes. In the initial stages of implementation, groups of volunteers from universities and relevant agencies worked for His Majesty. They visited hill tribes villages regularly, providing advice, demonstrations, and training on crop cultivation and animal farming. Apart from the volunteers, the Royal Project staff were stationed in highland communities to work closely with the local communities To support these efforts, the Royal Project Development Centres and Royal Agricultural Stations were established in various highland areas, which enable the Royal Project to reach the communities, understand their problems, and address their needs. Royal Project staff served as developers, addressing economic, social, and environmental issues through the operational units of the Development Centres and Agricultural Stations. The Royal Project has been implemented in accordance with His Majesty King Bhumibol Adulyadej the Great's wisdom on "Understanding, Access and Development" and His Majesty's philosophy on Sufficiency Economy for living.

Vegetable Plantation

Strawberry Plantation

The Royal Project's area covers six provinces in the North, namely Chiang Mai, Chiang Rai, Lamphun, Phayao, Mae Hong Son and Tak. Four Royal Agricultural Stations conduct research and development. Thirty-nine crop replacement promotion stations, known as the Royal Project Development Centres, have been established. The most recent centre established is the Ler Tor Royal Project Development Centre in Tak.

Products of the Royal Project

Over 55 years of implementation, the Royal Project Foundation has achieved remarkable success in carrying out the Royal Project, earning high appreciation from various countries. It has become a prototype for alternative highland development model, significantly reducing opium

poppy cultivation in Thailand. As a result, the United States removed Thailand from the list of opium poppy cultivation countries in 1999. By 2022, Thailand's opium poppy cultivation area had been reduced to only 17 hectares. The Royal Project Foundation operates alternative development programmes under the Strategic Plan, which provides a framework for its implementation. This plan aligns with the royal intention of His Majesty King Bhumibol Adulyadej The Great, benefiting highland cimmunities, the nation, in line with the National Strategy and the United Nations Sustainable Development Goals (UNSDGs). The Royal Project has made significant achievements in plant research, the development of coffee products, and the production of hemp weaving for textiles, with research extended to farmers living in other highland areas. Cultivating plants and raising animals on the highlands have helped farmers in Royal Project areas earn higher incomes above the poverty line. Moreover, the Royal Project has collaborated with the revevant government agencies to bring utilities and basic infrastructure to remote areas which lack essential facilities, significantly improving the living condition of hill tribe farmers.

Coffee Plantation

Vegetable Cultivation

Another Alternative Development Prototype

Doi Tung, 36 years ago, was a remote area where residents had no accessed to basic utilities or infrastructure. The local people lacked of agricultural knowledge and lived in poverty, which led them to rely on illegal activities, particularly opium poppy cultivation and trading with the ethnic minority groups. Many individuals became involved in the narcotic drug trade, drug consumption, and even prostitution in the hope of achieving a better livelihood. Significant changes began on 15 January 1987 when Her Royal Highness Srinagarindra, the late Princess Mother, visited Doi Tung for the first time. Her Royal Highness observed the dire conditions and recognized that poverty and a lack of opportunities were the root causes of the local people's struggles. In 1988, Her Royal Highness initiated the Doi Tung Development Project covering an area of 93,515 rai (14,962.40 hectares). The project was inspired by His Majesty King Bhumibol Adulyadej The Great's Royal Project and his royal initiatives on crop replacement to substitute opium poppy cultivation and integrated development.

The Doi Tung Development Project began with the concept of "Cultivating People," focusing on improving the quality of life for local communities step by step. This approach was based on the belief that if the Project could help the villagers break free from the vicious cycle of "Sickness, Poverty, and Ignorance," it would be possible to overcome various social issues and environment degradation driven by the need for survival. Her Royal Highness Srinagarindra's vision focused on transforming both the forest and the lives of hill tribes, emphasizing how people could coexist with the forest under the principle of "Cultivating Forest, Cultivating People." This involved stopping deforestation, shifting cultivation, and opium poppy farming by creating sustainable jobs for the local people. These jobs would provide sufficient income and enable the villagers to learn new techniques through their employment in various activities of the Doi Tung Development Project. The ultimate aim was to elevate the villagers' quality of life, fostering self-reliance and addressing poverty through a people-centered approach. This approach emphasized economic progress balanced with social security and environmental preservation. It sought to enhance better awareness of natural resources and the importance of environmental conservation. Achieving these goals required time and long-term implementation.

The work of Doi Tung Development Project is divided into three phases as follows:

Phase 1 : 1988 - 1993 (6 years)

The first phase aimed to stop shifting cultivation and opium poppy cultivation among the hill tribes. The Doi Tung Development Project began by fostering mutual understanding between the project staff and the hill tribes to secure their cooperation in developing the Doi Tung area. This phase focused on laying the physical foundation which included developing basic utilities and infrastructure, improving quality of life through job creation, enhancing health care, education, vocational training, and income generation, organizing community order, establishing administrative systems, and promoting tourism to attract visitors to Doi Tung.

Phase 2 : 1994 - 2002 (9 years)

The second phase focused on promoting appropriate occupations and livelihoods suited to the area's geo-social conditions while systematically and sustainably preserving the environment. It also emphasized developing production systems capable of competing in both national and international markets. The Doi Tung Development Project set a target to help villagers in the area earn an income of no less than 30,000 baht per person per year, improve theirquality of life, and eliminate narcotic drugs within the project area to ensure community safety. Periodic surveys were conducted to assess progress. A significant focus of Phase 2 was developing Doi Tung into a tourist destination that met international standards, with an emphasis on eco-tourism and the preservation of tribal arts and culture.

Phase 3 : 2003 - 2017 (15 years)

The third phase focused on helping villagers achieve self-reliance, preserving the environment systematically, and enabling self-governance at the village level. It also aimed to align local administration with Thai legislation. As villagers began earning sustainable incomes, they could contribute to the government by paying taxes, just like all Thai citizens.

The three phases of Doi Tung Development Plan supported development activities in economic and social aspect, local culture, and natural resources and environment management,

alongside the development of basic utilities and infrastructure. These efforts aimed to provide the local people with the utmost benefits of living together sustainably.

Over the 30 years of the Doi Tung Development Project's operation, the living conditions of the local villagers in the Doi Tung area changed tremendously. Villagers learned to cultivate cash crops such as coffee and macadamia, contributed to forest preservation, and actively helped monitor and prevent illicit drug trafficking and consumption in their communities. They also participated in various activities organized by Doi Tung Development Project, which promoted vocational training in agriculture, handicrafts, cooking, tourism, and working at the Doi Tung Coffee House.

Doi Tung Before Development

Doi Tung After Development

Products of the Doi Tung Development Project

The success of the Doi Tung Development Project has been widely recognized by international entities. In 2003, the United Nations Office on Drugs and Crime (UNODC) praised the Doi Tung Development Project as a key player in reducing narcotic crops cultivation and addressing poverty in a sustainable manner. UNODC awarded certification to Doi Tung products, recognizing the project's success in solving problems through peaceful and sustainable development methods.

Introduction of Alternative Development Prototype to the World

Thailand's long-term implementation of alternative development - spanning over 55 years by the Royal Project Foundation under Royal Patronage and more than 30 years by the Mae Fah Luang Foundation under Royal Patronage - serves as a model for addressing opium poppy cultivation and fostering sustainable development. Thailand is pleased to share its experiences and technical expertise in alternative development with interested countries or those facing similar challenges. Both the Royal Project Foundation and the Mae Fah Luang Foundation have shared their knowledge and technical expertise with many countries while also promoting Thailand's alternative development model on the global stage. This includes publicizing the model through various international forums, i particularly at the Commission on Narcotic Drugs, where exhibitions and presentations showcase Thailand's achievements, as well as other international conferences. The two Foundations have promoted Thailand's alternative development work to various countries, generating significant interest in Thailand's alternative development model as a solution to opium poppy cultivation. This model has evolved to support sustainable development for communities affected by narcotic drug problems, poverty, and other challenges related to social and economic well-being, as well as healthcare. Thailand's alternative development model has demonstrated its adaptability in fostering community development. The model also aligns with the United Nations Sustainable Development Goals (UN SDGs).

The Office of the Narcotics Control Board (ONCB), as the national central body on narcotics control, has continuously supported alternative development work since its establishment in 1976. The ONCB has adopted the royal initiatives of His Majesty King Bhumibol Adulyadej The Great as guiding principles for implementing alternative development. This has been achieved through cooperation and coordination with relevant government agencies, the Royal Project Foundation, the Doi Tung Development Project, and various international agencies that have provided assistance for alternative development to Thailand. Key international agencies include the United Nations Fund for Drug Abuse Control (UNFDAC), which later became the United Nations Office on Drug and Crimes (UNODC). The UNFDAC supported the Thai-UN Crop Replacement and Community Development Project (1971-1973) and the Thai-UN Highland Agricultural Marketing and Production Project (HAMP) (1980-1983). Germany's GTZ contributed to the Thai-German Highland Development Project for 17 years (1981 - 1998), while the Thai-UN Integrated Pocket Area Development Project, funded by Germany, was implemented from 1990 to 1994. Additional assistance came from Australia for the Narcotics Crop Cultivation Control Project and from the Netherlands for the Mae Sa Mai Integrated Watershed Development Project. Other sources of funding included contributions from the United

States, New Zealand, Sweden, Norway, Canada, and international non-government organizations such as the International Organization of Good Templars (IOGT).

The ONCB, in cooperation with the Royal Project Foundation, the Mae Fah Luang Foundation, and the Ministry of Foreign Affairs, has publicized Thailand's expertise in alternative development through exhibitions presented to the global community at international forums. One of the key forums is the Commission on Narcotic Drugs (CND), the annual meeting held at the United Nations Office in Vienna, Austria, to determine global policies on narcotics control. As one of the 53 members of the CND, Thailand organized its first exhibition to showcase its expertise in alternative development during the 53rd session of the CND in 2010. Since then, Thailand has continuously presented its work through exhibitions at the CND sessions. The most recent exhibition was organized during the 67th session of the Commission on Narcotic Drugs, held from 14 to 22 March 2024.

Thailand's Exhibition on Alternative Development in 2010

Thailand's Exhibition on Alternative Development in 2016

Thailand's Exhibition on Alternative Development in 2020

Thailand's Exhibition on Alternative Development in 2024

A significant event was the organization of an exhibition to celebrate 50 years of the Royal Project, titled "The 50-Year Journey on Alternative Development towards Sustainable Development," during the 63th session of the CND, held from 2 - 6 March 2020 at the Rotunda Hall of the Vienna International Centre (VIC), United Nations Office in Vienna, Austria. The exhibition was inaugurated by H.E. General Kampanat Ruddit, Privy Councilor and Chairman of the Executive Board of the Royal Project Foundation. Ms. Ghada Fathi Waly, Executive Director of UNODC, delivered a welcome address. Delegations attending the 63rd session of the Commission on Narcotics Drugs were invited to participate in the opening ceremony and visit the exhibition.

Apart from the exhibition, Thailand also organized a Side Event during the CND session, featuring panel discussions on topics related to alternative development. This was done in cooperation with the United Nations Office on Drug and Crime (UNODC) and member states implementing alternative development, such as Germany, Peru, Myanmar, Lao PDR, and Colombia. Additionally, Thailand facilitated expert meetings on alternative development and submitted draft resolutions on alternative development to the CND for adoption and implementation by member states.

Transfer of Experiences on Alternative Development to Foreign Countries

The Royal Project and the Mae Fah Luang Foundation have adhered to the royal initiatives of His Majesty King Bhumibol Adulyadej The Great and Her Royal Highness Srinagarindra, the late Princess Mother, in improving the quality of life for people in their areas, addressing poverty, reducing narcotic crop cultivation, and restoring natural resources and the environment in a sustainable manner. Both the Royal Project and the Mae Fah Luang Foundation have shared their long-term experiences and lesson learned in alternative development with foreign countries interested in adopting Thailand's successful alternative development model. The Royal Project transferred the concept of "Royal Wisdom," while the Mae Fah Luang Foundation focused on transferring implementation experiences under the "Doi Tung Development Model." These efforts can be summarized as follows:

The Royal Project shared its experiences in alternative development and engaged in technical cooperation with Afghanistan during 2005 - 2007. During 2007-2010, the Royal Project collaborated with Colombia on specific aspects of alternative development. Similarly, during 2009 - 2013, it provided technical cooperation on alternative development with Lao PDR in Udomxay Province. Those projects applied the Royal Project Model to develop the area and improve the quality of life for local people.

On 18 - 19 July 2022, the Royal Project Foundation and Highland Research and Development Institute (HRDI) organized an international seminar "Sustainable Highland Development (ISSHD) Responding to Challenges Beyond the New Normal," at the conference hall of the Royal Project Research and Agricultural Development Centre in Chiang Mai, as well as through an online platform. The objective of the seminar was to exchange experiences on highland development with foreign experts and to publicize highland development practices following the Royal Project Model, recognized as a best practice for holistic development. It also aimed to expand the knowledge and lessons learned to domestic agencies and foreign countries.

Moreover, the international seminar provided a platform for exchanging experiences on highland development with participants from foreign countries and international organizations, including the United Nations Office on Drug and Crimes (UNODC), Lao PDR, China, Peru, Nepal, Bhutan, and Taiwan through presentation showcasing achievements of farmers within the Royal Project areas.

The Mae Fah Luang Foundation under Royal Patronage has shared the experiences of the Doi Tung Development Project through the concept of the Doi Tung Model, which represents over 30 years of lesson learned and long-term experience. This model applied to other areas with the same goal of managing natural resources, improving the quality of life in economic and social aspects, and promoting communities' ability to achieve self-reliance in sustainable manner. The Foundation has also shared the Doi Tung Development Model with other countries interested in learning about the alternative development approach which places people at the center, following the royal initiative of Her Royal Highness Princess Srinagarindra, the late Princess Mother. The significant alternative development projects implemented in foreign countries are as follows:

In 2002, the Mae Fah Luang Foundation implemented a project in Myanmar, where large-scale opium poppy cultivation and illicit drug trafficking were prevalent. This situation significantly affected Thailand due to the long border shared by both countries. The Royal Thai Government adopted a policy to address the drug problem, particularly focusing on drugs originatingfrom neighboring countries. To support the initiative, the ONCB provided financial support of 25,600,000 baht project implementation in Myanmar. The Mae Fah Luang Foundation, in collaboration with Myanmar's central narcotics control agency, the Central Committee for Drug Abuse Control (CCDAC), and the Ministry of Progress of Border Areas, National Races, and Development Affairs, carried out the Ban Yong Kha Development Project. Ban Yong Kha, a village in Shan State, faced severed drug-related problem along with widespread diseases such as malaria, tuberculosis and scabies. The Mae Fah Luang Foundation prioritized long-term development, focusing on infrastructure and utilities, particularly water and agriculture, to ensure food security. Subsequently, efforts were expanded to generate income within the community, build a hospital and a school, train local volunteers in healthcare, and teach agricultural skills to students. The project, implemented during 2002 - 2004, covered 14 villages with a total population of 6,022 people. The Mae Fah Luang Foundation sent experts and staff to work alongside Myanmar authorities. The project successfully addressed the health crises, reducing the malaria death rate to 0 percent within less than three years. Yong Kha village achieved a stage where villagers could sustain their livelihoods without cultivating opium poppy and became self-reliant. Villagers were able to grow food crops and cash crops three times a year, ensuring sufficient food for their entire lives.

Animal Feed

Hospital Building

In furtherance of the success of the Ban Yong Kha Development Project, the Royal Thai Government, represented by the ONCB, Mae Fah Luang Foundation, Myanmar's Central Committee for Drug Abuse Control (the central narcotics control agency), and Myanmar's Ministry of Progress of Border Areas, National Races, and Development Affairs, jointly identified other areas still facing drug-related problems. The goal was to bring development to improve the quality of life and living conditions for the people in the areas of Ban Kyaw Pa, Ban Loi Payin and Ban Na Yaung in Mong Hsat township. This effort led to the implementation of the Thai-Myanmar Sustainable Livelihood Development Project in Mong Hsat area, near Ban Yong Kha and opposite Mae Fah Luang District in Thailand. The project covered an area of 24,774 hectares across 56 villages with a population of 12,844 people and was implemented over five years, during 2013 - 2017, with a budget of 350 million baht.

The project focused on improving basic healthcare by addressing key diseases such as malaria and tuberculosis, deploying mobile medical units, training volunteers, building a hospital and toilets, sending medical doctors, and developing water systems for drinking and domestic use. Additionally, the project promoted agricultural development by constructing weirs or a reservoirs, providing seeds, fruit tree seedlings, and economic forest plants, creating an animal fund, and offering agricultural training. The Project aimed to address fundamental problems faced by the local population, including poverty, poor living conditions, and low income. By solving these problems, the drug problem could be mitigated, and the border area would become more secure. Thailand and Myanmar jointly agreed to address problems in these high-risk border areas, ensuring collaborative efforts for long-term solutions. The project was well accepted with good cooperation from the people in the project's area.

Rice Field

Weir Building

At present, the Mae Fah Luang Foundation has been implementing the Thai-Myanmar Sustainable Alternative Livelihood Development Project in cooperation with Myanmar's Central Committee for Drug Abuse Control (CCDAC) and Ministry of Border Areas, National Races, and Development Affairs from 2014 to 2025. This Project was scaled up from the original alternative development projects in Tachileik and Mong Hsat, with the main goal of addressing rampant drug issues and drug trafficking in the region. It covers an area of 4,638.96 hectares in Naungtayar, Pinlaung District, Shan State, and 1,708.96 hectares in Tachiliek District, Shan State, serving a population of 26,953 people in Naungtayar and 7,462 people in Tachileik. The primary goal of the project is to continue efforts to reduce the drug epidemic and illicit drug trafficking through sustainable alternative development. At the initial stage, the Mae Fah Luang Foundation focused on establishing basic amenities, such as irrigation systems, improving rice yields to ensure food security, training veterinary staff, setting up livestock medicine funds, and promoting Napier grass cultivation as animal feed in order to enhance the quality of life of for the people. Moreover, the project promoted occupations suitable to the geo-social environment, such as maize cultivation as animal feed, as well as coffee and tea cultivation, to increase occupational opportunities for the local population.

Water System Building

Animal Feed

Road to the United Nations Guiding Principles on Alternative Development (UNGPs on AD)

The success of alternative development in addressing the opium poppy cultivation problem for over 50 years, coupled with the accumulated experience in this field, led to the idea of initiating guiding principles for those working in alternative development, drawing from Thailand's alternative development model. Thailand's experience, along with international experiences, was incorporated into the formulation of the United Nations Guiding Principles on Alternative Development (UNGPs on AD). Thailand, represented by the Mae Fah Luang Foundation, the Royal Project Foundation, the ONCB, and the Ministry of Foreign Affairs, collaborated with Peru's central narcotics control agency, the National Commission for Development and Life without Drugs (DEVIDA) - the institution in charge of formulating and implementing Peru's drug policies - to jointly submit a draft resolution titled "Promoting Best Practices and Lesson Learned for the Sustainability and Integrality of Alternative Development" to the 52nd session of the Commission on Narcotic Drugs (CND) in March 2009. The draft resolution was adopted as the Resolution 52/6 of the Commission. A key element of the resolution was prioritizing alternative development as a fundamental policy principle for sustainably reducing narcotic crop cultivation. It also recognized the role of developing countries that had implemented alternative development initiatives, gained expertise, and established best practices.

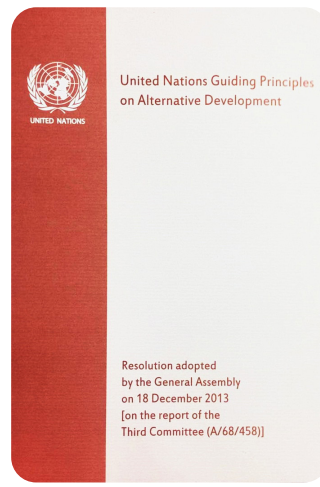
In 2010, Thailand and Peru jointly proposed hosting an international seminar and conference on alternative development in Thailand by submitting a draft resolution titled "Follow-up on the Promotion of Best Practices and Lessons Learned for the Sustainability and Integrality of Alternative Development Programmes" to the 53rd session of the Commission on Narcotic Drugs (CND). The resolution adopted the draft as Resolution 53/6, welcoming the offer by Thailand and Peru to co-host the international seminar and conference on alternative development. Initially scheduled for 12 - 19 November 2010, the conference was later postponed to 6 - 12 November 2011 and held in Chiang Rai and Chiang Mai under the name "International Conference on Alternative Conference (ICAD 1). The conference was attended by 104 participants, including experts and practitioners from 28 countries. It served as a platform to showcase Thailand's expertise in alternative development, including the Doi Tung Development Model and the Royal Project Model, and facilitated the exchange of knowledge on alternative development practices. The conference featured plenary sessions and working group sessions, focusing on initiating the draft International Guiding Principles on Alternative Development (INGP on AD) as a reference document and guideline for planning and implementing alternative development projects worldwide. The United Nations Office on Drugs and Crime (UNODC) provided secretarial support for the event. Participants also had the opportunity to pay study visits to the Doi Tung Development Project in Chiang Rai and at the Ang Khang Royal Agricultural Station of the Royal Project in Chiang Mai. The outcomes of the conference was reported at the 55th session of the Commission on Narcotic Drugs, held during 12 - 16 March 2012, and the Commission adopted Resolution 55/4, titled "Follow-up on the Proposal to Organize an International Workshop and Conference on Alternative Development." Later, Peru hosted the High-Level International Conference on Alternative Development during 14 - 16 November 2013 in

Lima, where the Lima Declaration on Alternative Development was agreed upon. The draft International Guiding Principles on Alternative Development was also adopted. These documents were subsequently submitted to the 56th session of the Commission on Narcotic Drugs, held during 11 - 15 March 2013, for acknowledgement and adoption. The report of the Commission was further submitted to the United Nations Economic and Social Council (ECOSOC) for adoption and later to the United Nations General Assembly at its 68th session. On 18 December 2013, and the General Assembly adopted the International Guiding Principle on Alternative Development (INGP on AD) as the United Nations Guiding Principles on Alternative Development (UNGP on AD), which were formalized as United Nations General Assembly Resolution 68/196.

ICAD 1

ICAD 2

Study Visit at Ban Yong Kha Project



United Nations Guiding Principles on Alternative Development (UNGPs on AD)

Salient Points from the United Nations Guiding Principles on Alternative Development

The United Nations Guiding Principles on Alternative Development propose actions and implementations measure in 38 points, summarized into the salient points as follows:

1. Mainstream Alternative Development as a part of long- term national development strategies and secure long-term political commitment and financing from governments and donor agencies:

To ensure continuity, alternative development programmes must secure long-term political and financial commitment from the governments. Equally important is gaining the support of local communities. Mainstreaming alternative development as part of national development strategies reflects a government's intention and commitment to improving the quality of life for its people, promoting peace, security, and the rule of law

2. Implement a holistic and balanced development approach, taking into account specific demographic, cultural, social and geographic conditions:

To address illicit narcotic crops cultivation and related issues, alternative development programmes must apply a holistic approach. This includes providing opportunities and improving the quality of life for local people to drive positive change in a sustainable manner.

3. Promote viable licit livelihood alternatives before deploying eradication measures toward narcotic crops cultivation, which is the main source of income:

Governments should consider proper sequencing when designing interventions to address illicit drugs issues. Since narcotic crop cultivation often represents the primary source of income for local people, development assistance must be provided before implementing law enforcement and eradication measures.

4. Ensure community participation and people-centred approach:

Alternative development programmes should not pre-design interventions without a thorough understanding of the local context. Planning development activities should be based on data collected on the ground and carried out in consultation with local communities and all relevant stakeholders.

5. Apply a resulted-oriented approach and measure the success of alternative development programme with human-centric indicators.

Success of drug policies is often measured by the number of illicit drugs cases or other law enforcement- related measures. However, these should not be the main criteria for evaluating alternative development programmes. Instead, alternative development should benefit stakeholders and be assessed using indicators that reflect improvements in human well-being and sustainable livelihoods.

6. Promote marketing strategies with access to domestic and international markets, encourage public-private partnership, and build entrepreneurial skills:

To create viable alternatives to illicit narcotic crops cultivation and other illegal activities, alternative development programmes must adopt a business mindset and market-oriented approach while improving local production capacity. These programmes should conduct research on domestic and international markets, as public-private partnerships can help accelerate the process and secure market access. Additionally, capacity building should focus on developing entrepreneurial skills such as profit and cost calculation, stock management, and basic marketing. Incubating local enterprises is an effective strategies for sustainable development.

7. Strengthening communities' ability to secure access to land and other production resources:

Access to production resources, particularly land, is fundamental for sustainable livelihoods but often causes conflict between governments and local communities. Local people reside in areas designated as national parks, which legally belong to the government, even though they have lived in there for generations before the laws were enacted. Shifting cultivation practices have also led to further encroachment into forest areas. A comprehensive land management strategy is needed to resolve conflicts and ensure a sustainable future for all stakeholders. This includes organizing areas into conservation forests, sustenance forests, economic forest, cultivation zones and residential areas, with consensus and understanding among local communities, local authorities, and the central government.

8. Protect the environment and empower local communities to conserve their traditional ways of life.

Alternative development programmes should enable local communities to benefit from natural resources, provided they are systematically managed and conserved for long-term sustainability. The introduction of new plant or animal species to generate additional incomes must consider impacts on existing species, climate conditions, and water resources. Development activities must avoid creating negative environmental impacts and should take into account traditional ways of life.

9. Promote peace, security, rule of law, and a culture of lawfulness.

Illicit drug problems cannot be tackled by law enforcement alone. It must go hand in hand with development assistance. Only when targeted communities are provided with opportunities and alternative livelihood can they transition away from the illicit economy. Alternative development programmes should play a role in promoting peace, security, and the rule of law, as these factors are essential for sustainability. The rule of law is not limited to enforcement but also involves fostering a culture of lawfulness within communities. Using a bottom-up approach, local people should actively participate in establishing community rules and regulations. The sense of ownership ensures that the rules are upheld, fostering law-abiding communities.

10. Promote continuous exchanges of best practices and innovative partnerships:

Alternative development programmes can advance by sharing best practices and lessons learned at regional and international levels. Events such as the Expert Group Meeting on Alternative Development (EGM on AD) United Nations platforms, study visits, and case studies of alternative development programmes are valuable tools for this exchange. Knowledge-sharing facilitates the practical application of the United Nations Guiding Principles on Alternative Development and other international guidelines, enabling further learning and collaboration among alternative development experts.

Translation of the United Nations Principles on Alternative Development into Practice

The adoption of the United Nations Principles on Alternative Development marked a global milestone, recognizing Thailand's leadership in alternative development as a sustainable solution to the drug problem. In 2014, the Royal Thai Government, represented by the ONCB, the Mae Fah Luang Foundation, the Royal Project Foundation, Highland Research and Development Institute (HRDI), the Ministry of Foreign Affairs, the Thailand Institute of Justice (TIJ), and other concerned agencies, agreed that Thailand should showcase its evidence-base of achievements in using development as a priority over law enforcement and eradication for sustainably addressing narcotic crop cultivation. These agencies also sought to advance efforts to promote the application of the United Nations Guiding Principles on Alternative Development in other countries, proving its effectiveness. Thailand proposed hosting the International Conference on Alternative Development II (ICAD 2) in cooperation with Myanmar, Germany, and the United Nations Office on Drug and Crimes (UNODC). The ICAD 2 was held during 18 - 24 November 2015 in Chiang Rai, Chiang Mai and Bangkok. The conference was divided into two parts: The Study Visits, held during 19 - 22 November 2015, and the High-Level Conference, held during 23 - 24 November 2015. During the study visit, participants observed alternative development in practice by visiting the Ban Yong Kha Project in Myanmar, the Doi Tung Development Project in Chiang Rai, where they exchanged experiences with project farmers,

and the Nong Hoi Royal Project Agricultural Development Centre in Chiang Mai, where they engaged with farmers in the Nong Hoi Royal Project area. The High-Level Conference, held at the Royal Orchid Sheraton Hotel in Bangkok, was graciously presided over by Her Royal Highness Princess Bajrakitiyabha, who also served as a panelist for the topic on "The Rule of Law and Security Challenges in the Development-Oriented Drug Control Context. The conference was attended by 258 participants from 38 countries and 17 organizations. Her Royal Highness also joined the panel as thepanelist for the topic on "The Rule of Law and Security Challenges in the Development-Oriented Drug Control Context. Major salient points from the study visits and conference included the recognition that alternative development is not a one-size-fits-all solution. A project successful in one area cannot be directly replicated in another; its planning and implementation must be tailored to the specific context and needs of the local communities. Moreover, the conference emphasized the importance of enhancing government and community participation, building trust between governments and communities, and fostering peace, the rule of law, and a culture of lawfulness. The ICAD 2 report was presented at the 59th session of the Commission on Narcotic Drugs (CND) in March 2016. its key recommendations were also used as inputs for the United Nations Special Session on the World Drug Problem (UNGASS), held during 19 - 20 April 2016 at the United Nations Headquarters in New York, USA.

Thailand has continuously promoted the utilization of the United Nations Principles on Alternative Development to many countries. For example, during the 61st session of the Commission on Narcotic Drugs (CND), held during 12 - 16 March 2018, Thailand cooperated with Peru to propose a draft resolution entitled "Promoting the Implementation of the United Nations Guiding Principles on Alternative Development and Related Commitments on Alternative Development and Regional, Interregional, and International Cooperation on Development-Oriented, Balanced Drug Control Policy Addressing Socioeconomic Issues" The resolution was adopted by the 61st session of the Commission.

Moving Forward with Sustainability

Thailand has consistently supported the implementation of the United Nations Guiding Principles on Alternative Development and has actively encouraged other countries to adopt the principles. This effort has been widely welcomed by many countries and the United Nations. On the occasion of the 10th anniversary of the United Nations Guiding Principles on Alternative Development in 2023, Thailand organized a side event during the 66th session of the Commission on Narcotic Drugs (CND), held during 13 - 17 March 2023. The side event titled "Hats on Hills: The Inclusive Pathway on Alternative Development for Sustainability," received support from Germany, Peru, the USA, the European Union, and the United Nations Office on Drugs and Crime (UNODC) Sustainable Livelihoods Unit. General Kampanat Ruddit, Privy Councilor and Chairman of the Royal Project Executive Board, along with other panelists, shared experiences on the Royal Project's work in developing areas previously affected by opium poppy cultivation. Their efforts emphasized conservation agriculture, which contributed to eliminating opium poppy cultivation while promoting soil conservation, forest restoration, and eco-system preservation. Additionally, Peru hosted the Expert Group Meeting on Alternative Development on

11 - 12 October 2023 in Lima, aiming to further support alternative development initiatives. The Commission on Narcotic Drugs also marked the 10th anniversary by organizing an intersession of its 66th session, held during 23 - 25 October 2023 in Vienna, Austria. This intersession brought together experts and practitioners in alternative development to commemorate the milestone and contributing to advancing the implementation of the United Nations Guiding Principles on Alternative Development.

Thailand, represented by the Ministry of Foreign Affairs and the Royal Project Foundation, submitted a draft resolution titled "Celebrating the Tenth Anniversary of the United Nations Guiding Principles on Alternative Development: Effective Implementation and the Way Forward" to the 67th session of the Commission on Narcotic Drugs (CND), held during 18 - 22 March 2024 at the Vienna International Centre in Vienna. The Commission adopted the draft resolution as Resolution 67/3, expressing concern over illicit narcotic crop cultivation, illicit drug manufacturing, and drug trafficking, which remain significant challenges in addressing and countering the world drug problem. The resolution emphasized the need to strengthen sustainable narcotic crop control and promote the application of the United Nations Guiding Principles on Alternative Development among member states to translate the principles into practice within their communities and among groups affected by narcotic crop cultivation and other drug-related activities. Thailand, through the Royal Project Foundation, announced its intention to host an international conference on the theme "From Alternative Development to Sustainable Development Goals: Empowering Alternative Development to Address Global Challenges" during 2 - 4 December 2024 in Chiang Mai. The conference provided an open platform for all interested parties to foster collaboration on alternative development. It also served as an opportunity to illustrate Thailand's achievements and leadership in alternative development, presenting its model as a prototype for further implementation at regional and global levels. The conference also aligns with the United Nations Sustainable Development Goals (SDGs).

The formulation of the United Nations Guiding Principles on Alternative Development was achieved through a comprehensive process aimed at elevating Thailand's alternative development model to the United Nations level. This long-term effort began with organizing forums and study visits to facilitate the exchange of experiences and lesson learned, showcasing Thailand's expertise in alternative development. The outcomes of these meetings was brought to the United Nations system via session of Commission on Narcotic Drugs (CND), where Thailand, as one of the 53 member states, leveraged its position to propose alternative development as a draft resolution. During these sessions, Thailand further promoted its alternative development work through exhibitions and side events, enabling foreign delegations to gain a clear understanding of Thailand's alternative development approach. Thailand received good cooperation from partner countries, which supported its efforts by jointly proposing draft resolution, co-sponsoring resolutions, co-hosting conferences and side events. The United Nations Office on Drugs and Crime (UNODC) provided particular support in these initiatives. Thailand has remained committed to promoting the United Nations Guiding Principles on Alternative Development to the interested countries. A significant achievement was theeffort by key Thai agencies - namely the Royal Project Foundation, the Mae Fah Luang Foundation, the Ministry of Foreign Affairs, and the Office of the Narcotics Control Board - to ensure that Thailand's alternative development model, based on the "Royal Initiative" of His Majesty King Bhumibol Adulyadej The Great and Her Royal Highness Princess Srinagarindra, the late Princess Mother, was integrated into the core elements of the United Nations Guiding Principles on Alternative Development. Moreover, the collective cooperation of these agencies in advancing sustainable alternative development has provided a model that can also be applied to broader community development efforts.

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Drug User Population: Findings from the 2024 Thailand National Household Survey

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Abstract

Understanding the current substance use situation is crucial for developing effective strategies to address its widespread impact. This study aims to estimate the size of the Thai population in 2024 engaged in drug use through a descriptive, cross-sectional household survey design employing a five-stage stratified cluster sampling method. For this study, Thailand was stratified into ten zones, with provinces, sub-districts, and communities systematically sampled within each zone. Households were selected systematically based on updated community maps, and within each household, participants were stratified by sex into two strata. A simple random sampling technique using a random number table was applied for each stratum, resulting in a total sample size of 34,410 individuals. Data collection was conducted between March and October 2024 through face-to-face structured interviews. The data were analyzed using frequency, percentage, mean, standard deviation, median, interquartile range, and point estimation to accurately represent substance use patterns across the Thai population.

In 2024, an estimated 3.7 million individuals in Thailand, representing 7.57% of the population aged 12 - 65, reported having experiences using narcotic substances at least once in their lifetime. Within the past year, approximately 1.9 million individuals, or 3.89%, reported drug use, while 1.2 million individuals, or 2.45%, indicated drug consumption within the past month. Among these recent users, approximately 330,000 individuals, or 0.67% of the population aged 12 - 65, were identified as regular users, defined as using drugs on 20 or more days in the past month. The most commonly used substances were Yaba (methamphetamine tablets), Ice (crystal methamphetamine), heroin, and ecstasy, in descending order of prevalence. Additionally, the survey reported 3.8 million kratom users and 1.6 million cannabis users across the country. These findings provide critical insight into the patterns of drug use in Thailand, underscoring the importance of targeted public health interventions, harm reduction strategies, and evidence-based policy responses to address the challenges associated with narcotic substance use.

Keywords: Narcotic Substances/Drugs, Prevalence, Thailand

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Introduction

Substance abuse remains a pressing global issue with far-reaching consequences for public health, social stability, and economic development. According to the United Nations Office on Drugs and Crime (UNODC), approximately 292 million individuals worldwide, aged 15 - 64 years, reported drug use in the past year as of 2022. Among these, 228 million individ-uals used cannabis, 60 million used opium, 30 million used amphetamines, 23.5 million used cocaine, and 20 million used ecstasy (UNODC, 2024). These statistics highlight the pervasive nature of drug use across diverse populations and underscore the urgent need for evidence-based interventions to address this complex and evolving challenge.

Historical evidence suggests that the use of psychoactive substances derived from plants dates back to approximately 50,000 BCE (Merlin, 2003). In Southeast Asia, the use of such substances can be traced back more than 15,000 years (Sullivan et al., 2002). Initially, these substances were primarily used for medicinal and ritualistic purposes, but over time, their use expanded to include recreational consumption.

In Thailand, historical evidence indicates that opium was introduced during the Sukhothai period. However, it was during the Ayutthaya period that the adverse societal impacts of opium use became evident, particularly as addiction impaired individuals' ability to sustain livelihoods. In response, King Ramathibodi I implemented punitive measures against opium use, codified in the Royal Code of Criminal Offenses in B.E. 1609 (Department of Fine Arts, 1978). Subsequent monarchs enacted a series of laws to regulate and control opium use. These included: The Act of Prohibiting the Purchase of Opium and Smoked Opium (Culasakaraj 1173 [1811]), The Decree of Prohibition of Smoking Opium (Culasakaraj 1181 [1819]), The Announcement of the Prohibition of Opium and Opium Smoking (Culasakaraj 1182 [1820]), The Act on Opium and Number Tattoo (Culasakaraj 1186 [1824]), The Opium Tax Act (B.E. 2414 [1871]), The Morphine and Codeine Act (B.E. 2456 [1913]), The Opium Act (B.E. 2464 [1921]), and The Narcotics Act (B.E. 2465 [1922]). Following Thailand's transition to a constitutional monarchy in 1932, drug control policies primarily relied on legal measures. Key legislative milestones included The Cannabis Act (B.E. 2477 [1934]), The Kratom Plant Act (B.E. 2486 [1943]), The Sale of Medicines Act (B.E. 2493 [1950]), The Revolutionary Council Announce-ment (No. 37) (B.E. 2501 [1958]), The Psychotropic Substances Act (B.E. 2518 [1975]), and The Narcotic Act (B.E. 2522 [1979]).

Despite these legislative efforts, the drug problem in Thailand has not diminished; instead, it has evolved. There has been a shift from natural addictive substances, such as opium, cannabis, and kratom, to synthetic drugs and the misuse of pharmaceutical substances. This transition underscores the persistent and adaptive nature of the drug epidemic, highlight-ing the need for comprehensive and dynamic policy measures to address both supply and demand-side challenges effectively.

The term "drugs" refers to any drugs or chemical compounds that influence an individual's physical and mental state when introduced into the body. In Thailand, the legal framework governing the regulation and control of these substances is primarily defined by four key legislative acts: The Narcotic Act, B.E. 2522 (1979) - aligned with the United Nations Single Convention on Narcotic Drugs (1961), which provides a comprehensive framework for controlling narcotic

substances. The Psychotropic Substances Act, B.E. 2559 (2016) - in accordance with the United Nations Convention on Psychotropic Substances (1971), focuses on the regulation of psychotropic drugs. The Decree on Prevention of Volatile Substances Use, B.E. 2533 (1990) - targets the misuse of volatile substances commonly used for inhalation. The Commodity Control Act, B.E. 2495 (1952) - addresses controlling and regulating specific chemical substances classified as commodities. It is important to note that these legislative instruments exclude certain legal substances, such as alcohol, tobacco products, and caffeinated beverages, which are regulated under separate legal provisions. This distinction underscores the specific focus of Thailand's drug control laws on substances with a high potential for abuse and dependence. In contrast, other commonly consumed legal substances remain outside their scope.

In 2019, the United Nations Office on Drugs and Crime (UNODC) reported that an estimated 275 million individuals aged 15 - 64 years, representing approximately 5.5% of the global population within this age group, had used drugs within the preceding year. Among these, 36.3 million individuals were identified as requiring treatment for substance use disorders (UNODC, 2021). During the same year, the ASEAN Drug Monitoring Report revealed that approximately 430,187 individuals in ASEAN member countries received drug treatment services, corresponding to a 65.6 per 100,000 population treatment rate. Notably, 73.8% of those treated were users of Amphetamine-Type Stimulants (ATS), while the remainder were treated for cannabis, opium/ heroin, and other substances (Kanato et al., 2020). Furthermore, a national household survey conducted by the Administrative Committee on Substance Abuse Academic Network estimated that approximately 1.91 million individuals, or 2.62% of the population aged 12 - 65 years, had used at least one illicit drug (including cannabis and kratom, excluding tobacco and alcoholic beverages) during 2019 (Kanato et al., 2020).

Comprehensive data on drug users, encompassing both legal and illegal substances, is essential for understanding the dynamic of the drug epidemic and serves as a foundation for developing evidence-based policies, implementing effective intervention strategies, and guid-ing further research to gain a clearer understanding of drug use patterns.

The first significant attempt to estimate the number of drug addicts in Thailand was undertaken in 1985 by Hirunrak and Piranpitak through the Estimating the Number of Drug Addicts from Informants: Pilot Project. This study, conducted in four provinces across four regions of the country, calculated both the number of drug addicts and the economic value of drug trafficking. The Key Informant Survey System was employed as the primary methodologi-cal tool. However, significant limitations in this approach hindered the effectiveness of the da-ta for guiding drug policy decisions.

In 1993, the Office of the Narcotics Control Board (ONCB), with support from the Narcotic Affairs Section of the U.S. Embassy in Thailand, commissioned the Thailand Develop-ment Research Institute (TDRI) to conduct a more comprehensive estimation of drug addiction in the country. This study focused on five significant substances: opium, heroin, cannabis, amphetamine/methamphetamine, and volatile substances. Utilizing a mixed-method approach, the research incorporated secondary data analysis, the Key Informant Survey System, random drug

testing, and target group interviews. The study, conducted across 16 provinces between 1993 and 1994, estimated a total of 1,267,590 drug addicts (Puapongsakorn et al., 1995). While this study provided valuable insights into the drug addiction landscape in Thailand, questions re-mained regarding the representativeness of the sample population and the complexity and accuracy of the estimation methodologies employed. These methodological limitations under-scored the need for refined approaches to ensure more robust and generalizable findings in future research.

In 2001, the ONCB sought to address the methodological limitations of the 1995 study by commissioning the Administrative Committee on Substance Abuse Academic Network (ACSAN) to conduct a nationwide household survey to estimate the prevalence of drug use in Thailand. This survey employed a multi-stage sampling method, aligning with the World Health Organization's (WHO) recommendation to utilize population-based surveys to collect robust and representative data on substance use. The 2001 survey focused on nine specific substances: opium, heroin, cannabis, kratom, methamphetamine, ecstasy, ketamine, cocaine, and inhalants. Data were collected from a sample population across 40 provinces, targeting individuals aged 12 - 65. The findings revealed that approximately 7,312,200 individuals nationwide reported having used at least one of these substances at some point in their lives, with 1,942,100 individuals identified as past-year users. The most commonly reported substances included methamphetamine, cannabis, kratom, inhalants, ecstasy, opium, heroin, ket-amine, and cocaine (ACSAN, 2001). This study provided a comprehensive overview of sub-stance use patterns in Thailand, offering valuable data for the formulation of evidence -based drug policies and highlighting the widespread prevalence of methamphetamine use as a critical area for intervention.

Following the 2001 national survey, the ONCB continued to commission the ACSAN to conduct subsequent nationwide household surveys to estimate the prevalence of drug use in 2004, 2007, 2008, 2011, 2016, and 2019 (ACSAN, 2004; ACSAN, 2007; ACSAN, 2008; ACSAN, 2011; Kanato et al., 2016; Kanato et al., 2020).

The ACSAN has conducted seven national household surveys, each contributing valuable data to inform evidence-based policymaking, preventive measures, and further research initiatives. These surveys have enabled the ONCB to comprehensively and systemati-cally understand drug use trends, facilitating targeted interventions and appropriate resource allocation.

However, the drug use landscape continues to evolve rapidly, with increased prevalence across diverse demographic groups, including adolescents, working-age adults, and both men and women. This ongoing transformation underscores the urgent need for updated data. As such, a nationwide survey to estimate the number of individuals involved in drug use is essential and necessary to be conducted again in 2024.

Objective

1. To estimate the number of drug users in Thailand in 2024.

2. To determine the prevalence of drug use categorized by type of substance abused.

Method

1. Study Design

This study employed a descriptive cross-sectional design using a nationwide household survey to estimate the prevalence and patterns of drug use in Thailand in 2024.

2. Population and Samples

2.1 Target Population:

The target population consisted of individuals of Thai nationality registered in the national population database. In 2024, the mid-year population was 64,753,796 people, of whom 49,055,591 were aged 12 - 65. Geographically, 16,652,219 resided in municipalities and Bangkok, and 32,403,372 resided outside municipalities. By gender, 24,148,152 were male, and 24,907,439 were female.

Of the 28,906,005 households in Thailand, the eligible target households were those on updated community maps and occupied by residents who had lived there for at least six months prior to the survey date.

2.2 Samples:

The study targeted Thai individuals aged 12 - 65 who had resided in the sampled households for at least three months within the previous year of the survey date. The final sample size included 34,410 individuals from 27 provinces across the country.

The sample size calculation considered prevalence rates ranging from 17.48 to 240.72 per 1,000 population, with an acceptable error margin of 1% and a design effect of 8.

2.3 Sampling Methodology:

A five-stage stratified cluster sampling method was employed to ensure national representativeness of the target population aged 12 to 65 years. Thailand was divided into 10 strata based on the ONCB operational regions: ONCB Bangkok (50 districts), ONCB Region 1 (9 provinces), ONCB Region 2 (8 provinces), ONCB Region 3 (8 provinces), ONCB Region 4 (12 provinces), ONCB Region 5 (8 provinces), ONCB Region 6 (9 provinces), ONCB Region 7 (8 provinces), ONCB Region 8 (7 provinces), and ONCB Region 9 (7 provinces).

First Stage: Systematic sampling with probability proportional to size (PPS) was used to select provinces/districts. A total of 27 provinces, including 17 districts in Bangkok, were selected.

Second Stage: Systematic PPS sampling was used to select 533 sub-districts based on the population size of the provinces /districts.

Third Stage: Systematic PPS sampling was used to select 1,165 communities /villages from the sampled sub-districts.

Fourth Stage: Using updated maps and household lists in the enumeration district, 17,205 households from the sampled communities were selected using systematic PPS sampling.

Fifth Stage: Within each household, individuals aged 12 - 65 were stratified by sex (male and female). Simple random sampling (using a random number table) was applied to select two individuals per household (one male and one female) who met the inclusion criteria and consented to participate in the survey. This resulted in a final sample size of 34,410 individuals.

TABLE 1: Summary of Sampling Stages

Stage	Sampling Unit	Number Selected	Sampling Method
1	Provinces/Districts	27	Systematic PPS
2	Sub-districts	533	Systematic PPS
3	Communities	1,165	Systematic PPS
4	Households	17,205	Systematic PPS
5	Individuals	34,410	Simple Random Sampling with a Random Number Table

This robust sampling approach ensures representative data collection to accurately estimate drug use prevalence across Thailand's diverse demographic and geographic aspects.

TABLE 2: Sample Sizes

Region	ONCB	Provinces	Districts	Sub-districts	Communities	Households	Samples
Central	1	Samut Prakan, Pathum Thani, Saraburi	20	52	104	1,746	3,492
Central	2	Chonburi, Chachoengsao, Prachinburi	18	40	89	1,312	2,624
Central	7	Ratchaburi, Nakhon Pathom, Samut Sakhon	15	44	82	1,376	2,752
Northeast	3	Nakhon Ratchasima, Buriram, Yasothon	40	84	207	2,865	5,730
Northeast	4	Udon Thani, Loei, Roi Et, Kalasin	46	90	206	2,836	5,672
North	5	Chiang Mai, Lampang, Chiang Rai	31	50	111	1,530	3,060
North	6	Nakhon Sawan, Tak, Phichit	25	53	110	1,629	3,258
South	8	Nakhon Si Thammarat, Krabi	23	37	76	1,160	2,320
South	9	Songkhla, Yala	17	41	92	1,293	2,586
BMA	BKK.	Bangkok	17	42	88	1,458	2,916
Total	10	27	252	533	1,165	17,205	34,410

3. Data Collection

Data collection for this study was carried out through structured face-to-face inter-views with randomly selected household members aged 12 - 65 using standardized data collection tools. The period spanned from March to October 2024, and the interviews were con-ducted by trained field researchers who had undergone comprehensive training to ensure consistency, accuracy, and ethical adherence.

The age group of 12 - 65 years was deliberately chosen because individuals under 12 years of age are generally less likely to have experience with substance use and may encounter communication barriers that hinder their ability to provide accurate responses. This age threshold aligns with international best practices for household surveys on substance use. Furthermore, evidence suggests that patterns of drug use differ significantly between males and females, with varying prevalence rates and substance preferences observed across genders. To ensure a comprehensive and representative dataset, the study intentionally included male and female participants within the 12 - 65 age range. This methodological approach aimed to capture nuanced patterns of substance use, enabling a more accurate assessment of drug use prevalence and trends across different demographic groups in Thailand.

3.1 Data Collection Teams:

The data collection process was carried out by six regional research teams, each responsible for specific geographical zones in Thailand:

Northeastern Region: A research team from the Center for Addiction Science at Wongchavalitkul University collected data in seven sample provinces.

Northern Region: A research team from the Health Sciences Research Institute, Chiang Mai University, oversaw data collection in six sample provinces.

Eastern Region: A research team from the Social Research Institute, Chulalongkorn University, managed data collection in three sample provinces.

Central Region: The College of Public Health, Chulalongkorn University, conducted data collection in three sample provinces.

Southern Region: Four sample provinces were assigned to a team from the Southern Academic and Research Network on Substance Abuse, Prince of Songkla University.

Bangkok and Western Region: The ISAN Substances Abuse Academic Network, Khon Kaen University, managed data collection in Bangkok and three sample provinces in the western region.

3.2 Data Collection Procedures:

Training and Preparation: Research assistants (field workers) underwent comprehensive training, including interview practice and assessment tests, to ensure they met minimum competency criteria before deployment.

Fieldwork Organization: Each data collection team comprised eight field staff members supervised by one field supervisor.

Participant Consent: Field staff explained the study's objectives to the sample groups to seek their consent to participate in the study and allowed them one day to decide whether to participate and sign in the consent forms, with the appointment to collect the forms scheduled for the following day. If participants were unavailable, appointments were rescheduled up to three times. After the third attempt, non-participation was recorded as a refusal to consent.

Data Validation: The field supervisor compiled interview forms every evening during

fieldwork. Another field staff member reviewed the forms for completeness and accuracy, and the supervisor performed a final inspection before submission to the central research team.

4. Data Management and Analysis

After data collection, the interview forms underwent systematic data management and analysis using statistical software. The process included the following key steps:

4.1 Data Validation:

The data were checked for completeness, missing values especially from the important questions, logical consistency, and clarity of handwriting or responses. Any inconsistencies or ambiguities identified were flagged for prompt correction to ensure data accuracy and reliability.

4.2 Data Coding:

A coding manual was developed, specifying codes for variables derived from closed-ended and open-ended questions. Data were systematically coded and categorized according to pre-established guidelines.

4.3 Data Entry:

Data were entered using the double -entry method, with two independent teams performing data entry to minimize errors. Duplication and discrepancy checks were conducted to identify and resolve data entry errors. Adjustments were carried out until the accuracy of the data were ensured.

4.4 Data Quality Assurance:

Data files were reviewed for out-of-range values, outliers, and missing data. Corrections and adjustments were made where necessary to enhance data quality.

4.5 Data Analysis:

The collected data were analyzed using descriptive and inferential statistical methods to comprehensively understand the drug use epidemic and patterns within the target population.

Descriptive statistical methods, including frequency, percentage, mean, median, standard deviation, and quartile range, were employed to summarize and describe the key characteristics of the study population across different demographic and geographic groups.

Point estimation methods were applied to estimate the number of substance users and the prevalence of substance use within the broader target population, providing statistically reliable projections based on the sampled data.

These analytical approaches ensured rigorous interpretation of the dataset, enabling the identification of substance use trends, demographic patterns, and regional variations. The findings are expected to offer evidence-based insights to inform policy devel-opment, intervention strategies, and resource allocation for addressing substance use issues in Thailand.

5. Ethics

This study received ethical approval from the Wongchavalitkul University Ethics Committee (Reference No. 050/2567). Informed Consent: Written informed consent was obtained from all participants, and in cases involving minors, consent was additionally secured from their parents or legal guardians. Confidentiality: Participants' data were treated with the utmost confidentiality and used exclusively for research purposes in compliance with ethical standards for human research.

This rigorous ethical framework ensured participant protection, data integrity, and adherence to international ethical research guidelines.

Results

Drug use remains a significant public health concern in Thailand, with recent data indicating that approximately 3.7 million individuals, or 75.74 per 1,000 people aged 12 - 65 years, have reported using at least one primary in their lifetime. Among the substances reported, Yaba (methamphetamine tablets) emerged as the most commonly used drug, followed by Ice (crystal methamphetamine), ecstasy, inhalants, heroin, ketamine, opium, and cocaine, respectively.

The term primary drug in this article refers to the primary target drugs, including Yaba, Ice, ecstasy, ketamine, cocaine, opium, heroin, and volatile substances, excluding kratom, cannabis, mixed substances, and other substances.

In Thailand, an estimated 1.9 million individuals, equivalent to 38.94 per 1,000 people aged 12 - 65 years, reported using at least one type of drugs within the past year. These individuals represent a critical demographic requiring ongoing public health surveillance and intervention. Among the substances reported, Yaba was identified as the most commonly used drug, followed by Ice, heroin, ecstasy, ketamine, inhalants, opium, and cocaine, respectively. These findings underscore the persistent dominance of methamphetamine-based substances in Thailand's drug use patterns emphasizing the need for targeted prevention strategies and prompt, effective responses. The results also emphasized the need for specific prevention strategies, harm reduction initiatives, and evidence-based policy measures to address the health and social consequences associated with drug use.

Thai population aged 12-65 years, approximately 1.2 million individuals, or 24.50 per 1,000 people, reported using at least one type of drugs within the 30 days preceding the survey. This group represents a key target population for brief interventions and community-based treatment programs aimed at mitigating the health and social consequences of substance use. The most commonly used drugs during this period were Yaba, followed by ecstasy, heroin, Ice, ketamine, opium, cocaine, and inhalants, respectively. These findings highlight the ongoing prevalence of methamphetamine derivatives as the primary substances of concern while also drawing attention to the emerging use of other drugs.

Habitual drug use, defined as consumption on more than 20 days within the past 30 days, is a critical indicator of substance dependence and highlights a population in urgent need of structured treatment interventions. In Thailand, approximately 330,000 individuals, or 6.74 per 1,000 people aged 12 - 65, fall into this high-risk category. These individuals typically exhibit patterns of drug use exceeding five days per week, suggesting a high likelihood of addiction. The most frequently used drugs among this group are Yaba, followed by ecstasy, heroin, Ice, ketamine, cocaine, opium, and inhalants, respectively. These findings emphasize the dominance of methamphetamine-based substances in patterns of chronic drug use and underscore the pressing need for comprehensive, evidence-based treatment programs.

TABLE 3: Number of Narcotic Substance Users and Prevalence Rate (per 1,000 population)

	Lifetime		Past Year		Past Month		20 Days within Past Month	
	Amount	Rate per 1,000 Pop.	Amount	Rate per 1,000 Pop.	Amount	Rate per 1,000 Pop.	Amount	Rate per 1,000 Pop.
Any substances	3,715,393	75.74	1,910,027	38.94	1,201,677	24.50	330,522	6.74
Meth amphetamine tablets	3,082,300	62.83	1,573,810	32.08	1,012,090	20.63	281,159	5.73
Crystal methamphetamine	801,669	16.34	174,249	3.55	51,502	1.05	10,775	0.22
Ecstasy	375,732	7.66	147,778	3.01	106,314	2.17	26,720	0.54
Ketamine	304,817	6.21	93,944	1.92	44,039	0.90	7,162	0.15
Cocaine	88,187	1.80	10,740	0.22	8,100	0.17	2,829	0.06
Opium	287,881	5.87	68,012	1.39	36,844	0.75	2,549	0.05
Heroin	323,338	6.59	152,646	3.11	73,475	1.50	15,831	0.32
Inhalants	358,534	7.31	76,813	1.57	4,857	0.10	1,246	0.03
Polydrugs	1,045,781	21.32	281,043	5.73	107,857	2.20	10,737	0.22
Mixed substances	84,105	1.71	21,623	0.44	2,480	0.05	1,802	0.04
Kratom	5,929,596	120.88	3,852,491	78.53	2,751,615	56.09	1,319,248	26.89
Cannabis	3,661,208	74.63	1,592,717	32.47	1,241,393	25.31	353,269	7.20

Polydrug use, defined as the concurrent or alternating use of two or more psychoactive substances, represents a significant public health concern due to its association with increased health risks and treatment complexity. In Thailand, approximately 1 million individuals, or 21.3 per 1,000 people aged 12 - 65 years, reported experien cing polydrug use at least once in their lifetime. Within the past year, approximately 280,000 individuals, or 5.73 per 1,000, reported polydrug use, while approximately 100,000 individuals, or 2.2 per 1,000, reported polydrug use within the 30 days preceding the survey. Of particular concern, approximately 10,000 individuals, or 0.22 per 1,000, reported frequent polydrug use, defined as consumption on more than 20 days within the past 30 days. The substances most commonly associated with polydrug use include Yaba, Ice, ecstasy, ketamine, cocaine, opium, heroin, and inhalants.

Understanding the demographic and socioeconomic profiles of drug users is essential for developing targeted interventions and evidence-based policies. In Thailand, approximately 1.9 million individuals reported drug use within the past year. Of these, 1.5 million (79.28%) were male and 390,000 were female, yielding a gender ratio of 3.82:1. The majority of drug

users (58%) are of working age (26 - 50 years), while 6.5% are children and youth (12 - 17 years), 22.5% are teenagers (18 - 25 years), and 12.4% are adults (51 - 65 years). This data reflects the prevalence of substance use among the workingage population, which may directly impact work efficiency and the country's economic productivity. In terms of household roles, 18.6% of drug users identified as heads of households, 50.9% as sons/daughters of the household heads, 4.9% as spouses, and the remainder as relatives or residents, reflecting the diverse roles and responsibilities of substance users within the household context. Marital status data indicated that 39% were married and cohabitating, while 46.6% were single. Education levels among drug users revealed that 32.9% had lower secondary education, 31.1% had primary education, 15.3% had upper secondary education, 12.5% had vocational education, and the remaining individuals held a bachelor's degree or higher. Occupational data showed that over half of the respondents were engaged in basic jobs (e.g., agricultural workers, taxi drivers, unskilled laborers), 10% were formal employees (civil servants, state enterprise workers, private employees), 22% were students or unemployed/ retired, and the remainder worked as merchants, freelancers, or in other sectors.

These findings provide a comprehensive demographic and socioeconomic profile of current drug users in Thailand, reflecting the diversity in educational levels and occupational statuses within the population group. This emphasizes the need for tailored prevention, treatment, and rehabilitation programs that address the unique needs of each subgroup within the population.

Mixed substances, characterized by the specified substance combinations such as Happy Water and ketamine milk powder, have become an escalating concern due to their heightened health risks and treatment challenges. In Thailand, approximately 84,000 individuals reported having used mixed substances at least once in their lifetime. Within the past year, this figure declined to approximately 21,000 individuals, while around 2,000 reported using mixed substances within the 30 days preceding the survey. Alarmingly, approximately 1,000 individuals indicated frequent use. These usage patterns suggest an emerging subset of high-risk users who may require specialized intervention and treatment strategies. Given the potential for severe health complications and the difficulty of managing polysubstance effects, targeted public health policies, enhanced surveillance, and evidence-based harm reduction strategies are urgently needed to promptly address this emerging trend.

In 2021, kratom (Mitragyna speciosa) was officially removed from Thailand's narcotics list, rendering its cultivation, possession, and consumption legal. This legislative shift has significantly impacted kratom usage patterns and behaviors across the population. A recent survey revealed that approximately 5.9 million individuals reported having used kratom at least once in their lifetime. Within the past year, approximately 3.8 million individuals reported kratom consumption, while around 2.7 million individuals indicated kratom use within the 30 days preceding the survey. Notably, frequent use—defined as kratom consumption on more than 20 days within the past 30 days—was reported by approximately 1.3 million indi-viduals. These findings underscore the prevalence of kratom use in Thailand, especially after the legislative shift, and highlight the importance of continuous monitoring of kratom use, as well as ongoing public health monitoring

and regulatory frameworks to address both the potential benefits and risks associated with its consumption. These frameworks should aim to balance the promotion of medical uses with the management of risks related to kratom abuse. Addi-tionally, further research is essential to develop a comprehensive understanding of both the short-term and long-term effects of kratom consumption.

In Thailand, the Ministry of Public Health officially announced the removal of all parts of the cannabis plant (Cannabis sativa) from the national narcotics list, effectively legalizing its cultivation, possession, and use in 2022. This policy shift has significantly influenced cannabis consumption patterns and behaviors among the Thai population. A national survey revealed that approximately 3.6 million individuals reported having used cannabis at least once in their lifetime. Within the past year, approximately 1.6 million individuals indicated cannabis use, while around 1.2 million reported use within the 30 days preceding the survey. Among these recent users, approximately 350,000 individuals were identified as frequent users, defined as consumption on more than 20 days within the past 30 days. These findings provide essential insights into cannabis consumption trends and patterns following a major legislative shift in Thailand, emphasizing the need for evidence-based policies and public health strategies to address both the benefits and potential risks associated with increased cannabis accessibility.

The World Health Organization's Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) serves as a standardized tool for assessing substance-related risk and guiding intervention strategies. In Thailand, an estimated 1.7 million individuals reported the use of amphetamine-type stimulants (ATS), including Yaba (methamphetamine tablets), Ice (crystal methamphetamine), and ecstasy. Approximately 260,000 individuals (15%) were classified as high-risk users, indicating the need for immediate entry into comprehensive treatment programs. Additionally, 1 million ATS users (60%) were identified as moderate-risk, requiring educational interventions on the adverse effects of ATS use and scheduled follow-up assessments.

Among opium and heroin users, approximately 250,000 individuals were screened, with 13,000 (5%) categorized as high-risk, necessitating intensive and immediate treatment. A further 120,000 individuals (49%) were classified as moderate-risk and require educational interventions and continued monitoring.

These findings highlight the urgent need for tailored public health strategies, including targeted treatment programs for high-risk groups and ongoing support and counseling for moderate-risk users. Evidence-based harm reduction initiatives and follow-up frame-works are essential to mitigate the health and social consequences of substance use in Thailand.

TABLE 4: Number of Substance Users Classified by Type of Drug and Level of Harm.

Level of harm	Bangkok	Central	North	Northeast	South	Total
ATS						
Low	36,485	234,444	95,070	27,808	44,157	437,963
Medium	14,659	131,390	230,351	605,743	82,360	1,064,502
High	7,249	7,734	2,742	233,458	15,459	266,643
Opiates/Opioids						
Low	998	35,336	66,401	9,223	965	112,922
Medium	19,022	17,297	78,674	4,281	0	119,274
High	10,043	1,995	670	273	0	12,982
Cocaine						
Low	12,574	20,065	1,855	0	0	34,494
Medium	4,833	2,727	547	29,531	0	37,638
High	0	0	0	0	0	0
Inhalants						
Low	12,319	81,318	50,469	30,924	1,026	176,056
Medium	5,589	2,055	2,171	706	0	10,521
High	0	0	0	0	0	0
Ketamine						
Low	6,020	104,697	1,841	42,557	0	155,115
Medium	12,321	8,874	32,724	0	0	53,919
High	0	1,802	0	273	0	2,075
Cannabis						
Low	9,306	116,834	120,520	27,090	21,931	295,681
Medium	21,395	47,774	60,028	52,676	35,013	216,886
High	12,135	13,736	0	59,893	1,175	86,939
Kratom						
Low	19,377	91,887	32,832	18,028	19,653	181,777
Medium	28,484	180,937	108,642	173,733	39,743	531,540
High	10,684	24,198	0	116,455	9,685	161,022

Substance use and mental health disorders are closely intertwined, posing significant challenges for healthcare systems. In Thailand, approximately 1.9 million drug users are estimated to experience some degree of mental health concern. Among them, 220,000 individuals

(12%) exhibit observable signs of mental illness, noticeable to family members and community members. An additional 640,000 individuals (33%) are identified as being at risk of developing mental health disorders due to prolonged substance use. Alarmingly, 860,000 individuals (45%) require formal psychiatric assessment and intervention at specialized treatment centers to ensure appropriate care.

Comprehensive treatment programs should include psychological therapy, pharmacological inter-ventions, and tailored psychosocial support systems for treatment and disease prevention. These findings highlight the critical need for an integrated approach that combines substance use treatment with mental health services to address the dual burden of addiction and psychological disorders effectively.

TABLE 5: Number of Substance Users and Psychological Risk

	Bangkok	Central	North	Northeast	South	Total
Any substances						
Current users	78,297	431,643	385,925	871,631	142,531	1,910,027
Users with Psychological symptoms	7,111	69,833	36,405	65,597	41,542	220,487
Users who are at risk of Psy. symptoms	58,115	221,794	88,395	166,567	104,373	639,243
Methamphetamine tablets						
Current users	44,300	274,212	256,073	857,250	141,976	1,573,810
Users with Psychological symptoms	7,111	67,047	25,051	64,739	41,542	205,489
Users who are at risk of Psy. symptoms	25,116	141,886	50,862	164,058	104,373	486,294
Kratom						
Current users	33,718	224,780	82,621	218,452	55,270	614,841
Users with Psychological symptoms	0	29,407	5,929	5,608	20,468	61,412
Users who are at risk of Psy. symptoms	26,231	130,908	20,507	43,740	40,588	261,974
Cannabis						
Current users	28,957	59,704	77,757	91,799	39,133	297,349
Users with Psychological symptoms	0	12,471	9,950	9,155	3,150	34,726
Users who are at risk of Psy. symptoms	1,089	5,728	6,818	5,602	67,562	73,164

Discussion

Drug use remains a significant public health concern in Thailand, with approximately 1.9 million individuals, or 3.9% of the population, reporting having used at least one type of substance in 2024. Among these users, methamphetamine tablets (Yaba) remain the most prevalent substance, with approximately 1.6 million users. This is followed by over 170,000 users of Ice (crystal methamphetamine), more than 150,000 heroin users, nearly 150,000 ecstasy users, and fewer than 100,000 ketamine users. The remaining users reported consumption of volatile substances, opium, and cocaine. Although the number of users in this latter group is relatively low, these substances still pose significant health and social risks.

Furthermore, approximately 280,000 individuals reported polydrug use, defined as the concurrent or alternating use of two or more substances. These findings emphasize the persistent dominance of methamphetamine-based substances in Thailand's drug landscape and the rising concern of polydrug use, which complicates treatment and intervention strategies. Given the potential severe health risks and unintended clinical outcomes associated with poly-narcotic substance use, targeted policies, evidence-based harm reduction approaches, and comprehensive treatment programs are urgenttly needed to address the health and social consequences of these patterns of substance use.

Methamphetamine use remains a dominant public health challenge in Thailand, with evidence indicating a sharp increase in both prevalence and frequency of use between 2019 and 2024. The number of Yaba users rose from approximately 650,000 in 2019 to 1.5 million in 2024, reflecting a 2.5-fold increase. This surge can be attributed to higher rates of relapse, the initiation of new users, and a noticeable shift from other substances to Yaba. Notably, the number of past-30-day users tripled from 330,000 to 1 million, underscoring the growing accessibility, affordability, and widespread availability of Yaba in 2024.

Frequent Yaba use, defined as consumption on 20 or more days in a 30-day period (or at least five days per week), also witnessed a significant rise, increasing from 91,000 in 2019 to 280,000 in 2024. This pattern indicates an escalation in habitual use and a heightened risk of addiction, along with an increase in psychiatric comorbidities among users. Additionally, it is associated with the prevalence of comorbid psychiatric disorders among individuals with persistent drug use. These trends highlight the urgent need for comprehensive intervention strategies, including accessible treatment programs, robust harm reduction measures, and integrated mental health services to address both dependency and associated psychological disorders. The integration of these approaches will help address the complexities of persis-tent methamphetamine use and its associated mental health disorders.

Heroin use in Thailand has shown a significant upward trend, with the number of users increasing 1.7-fold from approximately 93,000 in 2019 to 150,000 in 2024. This rise suggests broader exposure to heroin across diverse population groups, potentially driven by increased curiosity, experimentation among new users, and a resurgence in the popularity of the substance. The upward trend may also indicate shifts in drug market dynamics, including increased availability and changes in distribution networks.

These findings highlight an emerging public health concern, emphasizing the need for proactive intervention strategies. Comprehensive harm reduction programs, targeted prevention campaigns, and accessible treatment services

must be prioritized to address the growing prevalence of heroin use. Additionally, enhanced surveillance and research into the underlying factors contributing to this rise are essential for informing evidence-based policies and improving prevention and rehabilitation measures to reduce associated health and social burdens.

Since the conclusion of Thailand's "War on Drugs" in 2003, methamphetamine (Yaba and Ice) has emerged as the most prevalent and persistent narcotic substance in the country. An analysis of prevalence trends from 2003 to 2024 reveals two distinct phases. In the first decade (2003 - 2011), Yaba prevalence remained relatively stable, fluctuating between 0.70 and 2.00 per 1,000 population, reflecting a degree of control following the proactive policies implemented during the War on Drugs. However, in the subsequent decade (2011 - 2024), prevalence rates surged approximately 17-fold, rising from 1.91 to 32.08 per 1,000 population by 2024.

This sharp escalation indicates a significant increase in Yaba accessibility, affordability, and social acceptability, coupled with inadequacies in both prevention and treatment frameworks resulting in an incomprehensive solution to its prevalence. Moreover, the data suggests persistent gaps in law enforcement effectiveness, allowing Yaba distribution networks to expand. These trends underscore the urgent need for a multi-sectoral approach that integrates evidence-based prevention strategies, scalable treatment programs, and strengthened law enforcement measures to address the root causes driving methamphetamine proliferation in Thailand.

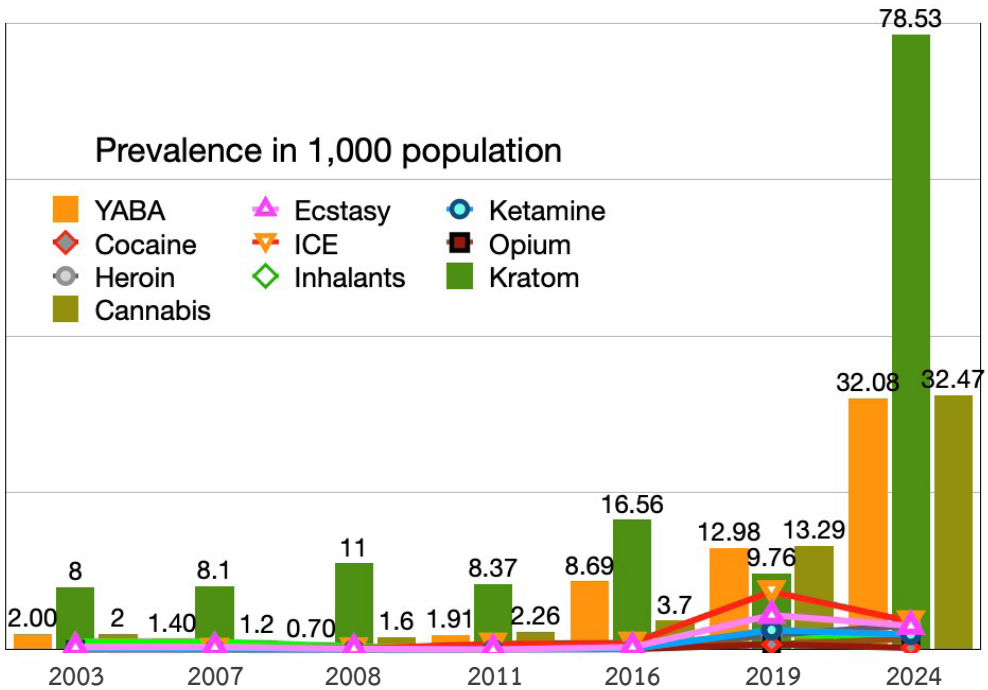

Figure 1 Trends of Substance Abuse Epidemic (per 1,000 population).

Heroin use in Thailand has experienced a dramatic resurgence over the past two decades, reflecting broader trends observed across other illicit substances. Between 2003 and 2011, heroin prevalence remained consistently low, below 0.01 per 1,000 population. However, in the subsequent decade (2011 - 2024), the prevalence rate increased 62-fold, from 0.05 to 3.11 per 1,000 population. This sharp escalation suggests increased availability, evolving drug market dynamics, and a potential shift in user preferences.

The pattern observed in heroin prevalence mirrors trends seen with other illicit drugs, where a significant increase followed low baseline prevalence in use. Simultaneously, a decline in the prevalence of certain substances suggests a phenomenon of substance substitution, with users transitioning to more accessible or cost-effective alternatives.

These findings highlight the urgent need for comprehensive public health responses, including targeted prevention campaigns, accessible harm reduction initiatives, and integrated treatment programs tailored to address opioid dependence. Furthermore, law enforcement strategies must adapt to the shifting patterns of drug distribution and consumption to effectively curb the growing heroin epidemic in Thailand.

The legislative amendments decriminalizing cannabis and kratom in Thailand between 2021 and 2022 have significantly influenced patterns of use across various demographic groups. Following legalization, national surveys revealed an observable increase in the preva-lence of both cannabis and kratom use, particularly among children, youth, and adults. This rise is attributed to recreational and medical purposes, facilitated by reduced legal barriers and increased social acceptance. Which has, in turn, diminished the social stigmatization associated with cannabis and kratom use.

Notably, the Ministry of Public Health reported a substantial increase in the number of individuals registering for medical cannabis use. This trend corresponds with improved accessibility to certified clinics and hospitals offering cannabis-based treatments. While legali-zation has expanded therapeutic opportunities, it has also raised concerns about potential misuse, especially among younger populations. Who are at high risk of adverse health effects from the use of cannabis and kratom.

These findings emphasize the need for robust regulatory frameworks, to ensure responsible use of the substances within the legal frameworks. Additional recommended measures include public education campaigns, and comprehensive monitoring systems to ensure responsible use, minimize misuse, and maximize the public health benefits of legalized cannabis and kratom.

The increasing prevalence of drug use in Thailand, particularly among children, youth, and working-age populations, underscores the urgent need for a multi-faceted approach to address this public health crisis. Based on recent survey findings, this study provides key recommendations across five strategic areas: prevention, treatment, law enforcement, research, and policy development.

1. Prevention:

Survey results highlight rising drug use among children, youth, and working-age individuals. Effective prevention strategies should include targeted educational campaigns in schools, focusing on the harmful effects of drugs, enhancing decision-making skills, and developing resilience against peer pressure. Families and communities play a pivotal role in monitoring behaviors,

fostering supportive environments, and serving as protective barriers against drug initiation.

2. Treatment and Rehabilitation:

Given the increasing number of drug users, emphasis must be placed on comprehensive and standardized treatment programs. These should integrate medical interventions, psychological counseling, and vocational training to reduce relapse rates. Accessible and community-linked rehabilitation centers are essential for ensuring sustained recovery and successful reintegration into society.

3. Law Enforcement:

Stringent measures should be applied to disrupt drug distribution networks at all levels. However, policies must clearly distinguish between drug users and traffickers. Small-scale users should be given opportunities for treatment and rehabilitation rather than punitive measures. While drug dealers should be prosecuted in accordance with the law. Continuous training programs for law enforcement personnel are essential to enhance their capacity to investigate drug-related offenses and understand evolving trafficking practices.

4. Research:

Continuous data collection and research are vital to understanding emerging drug-use trends, including shifts in drug types, consumption patterns, and associated health and social impacts. Evidence-based insights will guide the development of adaptive and effective policy and strategy responses to promptly address newly arising challenges.

5. Policy Development:

Drug policies must remain dynamic, reflecting current socioeconomic realities such as changes in drug markets, regional drug trafficking trends, and legislative frameworks. Policies should integrate prevention, treatment, law enforcement, and rehabilitation into a cohesive national strategy to ensure a comprehensive response.

Addressing Thailand's drug problem requires an integrated and multi-sectoral ap-proach encompassing effective prevention, accessible treatment, effective law enforcement, ongoing research, and adaptive policy development. Collaboration among stakeholders—including government agencies, healthcare providers, law enforcement, educational institutions, and communities—is critical to creating sustainable solutions and improving the quality of life for affected individuals and society.

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Heroin epidemic situation among juveniles

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Abstract

Background Since 2017, the number of juveniles undergoing heroin treatment has increased. In 2022, Thailand legalized cannabis for medicinal use and allowed the growing of cannabis. Using cannabis can be the gateway drug for heroin users. Thus, heroin use and associated behaviors among teenagers have become a topic of interest in order to prevent it from becoming a significant issue. Heroin dependents are not only an effect on their families and communities but, importantly, a crucial impact on one's physical health, resulting in premature deaths and an increased risk of overdoses. Additionally, injecting heroin can lead to HIV infection.

Objective To study the problem of the heroin epidemic among juveniles aged 12-25 years in order to set up preventive training programs against heroin dependence among juveniles.

Research Method This study used the snowball technique with purposive sampling, interviewing individuals aged under 25 years old with heroin-using experience in high-prevalence provinces, i.e., Chiang Mai, Chiang Rai, Bangkok, and Samut Prakan, resulting in a total sample size of 137.

Results More than 90% of the respondents were male, 81% were aged between 18-25 years, most lived with their parents and family, and over 70% are Buddhist. The majority had completed primary and lower secondary education, were single, and mostly worked irregular jobs with an average monthly income of 7,588 Baht. Most started trying heroin for the first time between the ages of 16-20, with the youngest starting at 12 years old. More than half used only heroin, and very few used heroin by injection, which was about 12%. The majority had never undergone treatment, and nearly half of them had been arrested for drug-related offenses. The reasons for becoming dependent on heroin included curiosity, being persuaded or pressured by family, friends, partners, or close acquaintances. About 5% used heroin as a way to avoid problems, such as relieving stress or discomfort. Qualitative data indicated that the main source of drugs came from friends or acquaintances within the community or nearby village and also receiving them for free from friends. Some of them had become drug dealers. About 10% had experiences being overdosed, and about 17% had seen some friends being overdosed. Half of the respondents had never undergone treatment. The health impacts were not yet comprehensible, but it was noticeable that many believed their dependence on drugs did not cause any trouble for society/community. However, the greater number wanted to abstain from heroin and believed that their families could help them.

Conclusion and Recommendations From the study, it was found that the epidemic evidently occurred among juveniles. Immediate action should be taken to prevent the younger generation who have not yet tried drugs and those who have used and have gained knowledge and understanding about the harmfulness of heroin use. Those who have already used should be advised to an appropriate treatment program. It is recommended that family members attentively watch over them.

Introduction

Currently, drug abuse is widely recognized as an escalating issue, with the number of users continuing to rise. According to the UNODC's World Drug Report 2024[1], in 2022, cannabis was the most commonly used substance globally, with 228 million users reporting usage within the past year. This was followed by opioids, including opium, heroin, morphine, and various painkillers, with 60 million users, and amphetamine-type stimulants (ATS), such as methamphetamine, crystal meth, ecstasy, and other central nervous system stimulants, with 30 million users. When compared to 2020, the number of global drug users has increased. The World Drug Report 2022[2] recorded 209 million cannabis users, 61 million opioid users, and 27 million ATS users over the previous two years. While the number of opioid users has slightly decreased, the health impacts remain significant. Opioids account for 69% of drug-related deaths and 40% of individuals seeking treatment. Opioid abuse has led to a loss of 12.9 million users due to illness or premature death, representing 71% of healthy years lost globally due to drug-related health impairments[3].

In Thailand, although there is no calculation of health loss and mortality caused by the use of opiates, there is data regarding the effects of heroin use. According to the 2017[4,5], harm reduction assessment report on drug injection, approximately 25% of heroin injectors were still infected with HIV. Additionally, about 17% reported experiencing an overdose, and among this group, approximately 70% of those who had overdosed died, which is a very high rate. In a recent study conducted in 2021[6], 32.6% of sampled heroin injectors had undergone HIV testing within the past six months, with less than 10% testing positive for HIV. It was observed that individuals under the age of 25 were more likely to undergo HIV testing, and women were more likely to get tested than men.

According to the National Narcotics Treatment and Rehabilitation Data System[7], the number of individuals receiving treatment between fiscal years 2019 and 2023 decreased

[1] World Drug Report 2024. https://www.unodc.org/unodc/en/press/releases/2024/June/unodc-world-drug-report-2024_-harms-of-world-drug-problem-continue-to-mount-amid-expansions-in-drug-use-and-markets.html

[2] World Drug Report 2022. https://www.unodc.org/res/wdr2022/MS/WDR22_Booklet_2.pdf

[3] UNODC, responses to the annual report questionnaire; and Institute for Health Metrics and Evaluation, "Global Burden of Disease Study 2019 Data Resources: GBD Results Tools.". (For a more detailed description of disability-adjusted life years (DALYs), see World Drug Report 2021, booklet 2).

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[7] Office of Narcotics Control Board. Drug Dependence Treatment Data from National Narcotics Treatment and Rehabilitation Data System (Fiscal year 2019-2023). Assessed date 3rd January 2024.

by approximately 35% (from 240,486 individuals in 2019 to 159,997 in 2023). This decline is attributed to a decrease in treatment-seeking among users of kratom and cannabis, which have been legalized. Conversely, the number of individuals receiving treatment for heroin use more than doubled, increasing from 1.5% to 3.9% of total cases. In absolute terms, this represents an increase from 3,616 individuals in 2019 to 6,160 individuals in 2023. Approximately 30% of these were new treatment cases. Most of the individuals receiving treatment were concentrated in Chiang Mai, Chiang Rai, and Bangkok, with the highest numbers reported at 1,167, 1,107, and 840 individuals, respectively. Given the evident health risks associated with heroin use, including mental health issues similar to those caused by methamphetamine, it is essential to study the epidemic of heroin use, particularly among youth who are at risk of initiating drug use in order to develop community-based prevention programs.

Methodology

This study used a snowball technique and purposive sampling, focusing on heroin users under the age of 25 in high-prevalence provinces, i.e., Chiang Mai, Chiang Rai, Bangkok, and its vicinity. Both quantitative and qualitative, in-depth interviews were collected. Using an effect size of 0.3 and a statistical power of 95%, the calculated sample size was at least 134 heroin users. The actual data collection included 137 individuals under the age of 25 with heroin use experience. Data collection was conducted between June and August 2023.

Results

1) Data Collection Areas

Data collection was conducted in communities where heroin users resided across 4 provinces, including Chiang Rai: 4 communities, Chiang Mai: 3 communities, Bangkok: 1 community and 4 clinics/health service centers, Samut Prakan (vicinity area): 1 health service center. In total, data was gathered from 13 locations.

2) Socio-Demographic Characteristics

Among the 137 participants: Gender: 124 were male (90.51%) and 13 were female (9.49%). Age: 26 participants (18.98%) were under 18 years old, while 111 participants (81.02%) were aged between 18-25 years. Most lived with their parents (79 participants, 57.66%), followed by those living with other relatives, such as grandparents or siblings (42 participants, 30.66%), and the remainder lived with partners/spouses or friends. Religion: The majority were Buddhists (90 participants, 65.69%), followed by Christians (38 participants, 27.01%). Education: Over 70% had completed primary or lower secondary school, with 15% still in school. Marital Status: Most participants (77.37%) were single. Employment and Income: 27.74% were unemployed, with half of the participants in Bangkok being jobless. The average monthly income was 7,588 baht.

Table 1 Socio-demographic characteristics

	Chiang Rai		Chiang Mai		Bangkok		Samut Prakan		Total	
	n	%	n	%	n	%	n	%	n	%
1.1) Gender										
Male	26	100.0	26	92.86	59	86.76	13	86.67	124	90.51
Female	0	0.00	2	7.14	9	13.24	2	13.33	13	9.49
Total	26	100.0	28	100.0	68	100.0	15	100.0	137	100.0
1.2) Age										
LT <18 years	3	11.54	13	46.43	8	11.76	2	13.33	26	18.98
18-25 years	23	88.46	15	53.57	60	88.24	13	86.67	111	81.02
Total	26	100.00	28	100.00	68	100.00	15	100.00	137	100.00
*Range 12-25 years old; Mean age 21.23 years old										
1.3) Living Arrangements										
Parents/Father/Mother	19	73.08	21	75.00	32	47.06	7	46.67	79	57.66
Partner/Spouse	0	0.00	0	0.00	14	20.59	0	0.00	14	10.22
Friends	0	0.00	0	0.00	2	2.94	0	0.00	2	1.46
Others	7	26.92	7	25.00	20	29.41	8	53.33	42	30.66
Total	26	100.00	28	100.00	68	100.00	15	100.00	137	100.00
1.4) Religion										
Buddhist	13	50.00	3	10.71	60	88.24	14	93.33	90	65.69
Islam	0	0.00	0	0.00	8	11.76	0	0.00	8	5.84
Christianity	12	46.15	25	89.29	0	0.00	0	0.00	37	27.01
Others	1	3.85	0	0.00	0	0.00	1	6.67	2	1.46
Total	26	100.00	28	100.00	68	100.00	15	100.00	137	100.00
1.5) Education status										
Primary level	8	30.77	15	53.57	23	33.82	6	40.00	52	37.96
Lower secondary level	8	30.77	6	21.43	26	38.24	6	40.00	46	33.58
Upper secondary level	1	3.85	2	7.14	7	10.29	0	0.00	10	7.30
Vocational certificate	0	0.00	1	3.57	3	4.41	0	0.00	4	2.92
Never studied	1	3.85	3	10.71	0	0.00	0	0.00	4	2.92
Currently studying	8	30.77	1	3.57	9	13.24	3	20.00	21*	15.33
Total	26	100.00	28	100.00	68	100.00	15	100.00	137	100.00

Table 1 Socio-demographic characteristics (cont.)

	Chiang Rai		Chiang Mai		Bangkok		Samut Prakan		Total	
	n	%	n	%	n	%	n	%	n	%
1.6) Marital status										
Single	26	100.00	26	92.86	41	60.29	13	86.67	106	77.37
Co-habiting	0	0.00	0	0.00	21	30.88	2	13.33	23	16.79
Separated	0	0.00	0	0.00	5	7.35	0	0.00	5	3.65
Divorced	0	0.00	2	7.14	1	1.47	0	0.00	3	2.19
Total	26	100.00	28	100.00	68	100.00	15	100.00	137	100.00

3) Heroin Use, Related Behaviors, and Consequences

3.1) Experience using heroin

All 137 participants had experience using heroin, with the following findings: age of first use - most first used heroin between the ages of 16-20 (80 participants, 58.39%), followed by those under 15 years old (43 participants, 31.39%) and those aged 21-25 (14 participants, 10.22%), respectively. The youngest aged of first use was only 12 years old.

Previous substance use to heroin; most participants reported smoking cigarettes prior to heroin use (75 participants, 54.74%). Other substances used prior to heroin included methamphetamine (50 participants, 36.50%), cannabis (44 participants, 32.12%), and kratom (43 participants, 31.39%). Noticeably, participants in Bangkok and Samut Prakan predominantly used cannabis (44.12% and 53.33%, respectively) before transitioning to heroin, while those in northern provinces typically started with cigarette use. Route of administration: injection was rare, with only 12.41% using this method. The majority smoked heroin (52.55%), followed by snorting or inhaling (35.04%). Despite using heroin for approximately 1-2 years, about half of the participants had never sought treatment. Conversely, nearly half (48.18%) reported having been arrested or prosecuted for drug-related offenses.

A study found that among 93 respondents, 67.88% reported using heroin for the first time out of curiosity and a desire to experiment. Following this, approximately one-quarter of the respondents were influenced by friends, partners, or close acquaintances. Interestingly, around 5% turned to heroin as a way to cope with problems, such as reducing stress or alleviating discomfort. A small proportion (1.46%) reported first-time heroin use due to coercion or because it was part of their job, such as being a drug retailer.

Table 2 Heroin Use

	Chiang Rai		Chiang Mai		Bangkok		Samut Prakan		Total	
	n	%	n	%	n	%	n	%	n	%
2.1) Age at first heroin use*										
10-15 years	11	42.31	15	53.57	13	19.12	4	26.67	43	31.39
16-20 years	14	53.85	12	42.86	46	67.65	8	53.33	80	58.39
21-25 years	1	3.85	1	3.57	9	13.24	3	20.00	14	10.22
Total	26	100.00	28	100.00	68	100.00	15	100.00	137	100.00
* Mean age of first use: 17.21 years; youngest age of first use: 12 years.										
2.2) Drug use prior to heroin**										
Kratom	2	7.69	4	14.29	34	50.00	3	20.00	43	31.39
Cannabis	1	3.85	5	17.86	30	44.12	8	53.33	44	32.12
Cigarette	13	50.00	25	89.29	30	44.12	7	46.67	75	54.74
Ketamine	0	0.00	0	0.00	10	14.71	3	20.00	13	9.49
Methamphetamine	12	46.15	15	53.57	21	30.88	2	13.33	50	36.50
Cough mixture	2	7.69	2	7.14	12	17.65	1	6.67	17	12.41
Ice	1	3.85	0	0.00	3	4.41	1	6.67	5	3.65
Ecstasy	0	0.00	0	0.00	3	4.41	1	6.67	4	2.92
Cocaine	0	0.00	0	0.00	2	2.94	2	13.33	4	2.92
Inhalants	1	3.85	4	14.29	6	8.82	3	20.00	14	10.22
Alcohol	3	11.54	10	35.71	13	19.12	3	20.00	29	21.17
Never use drugs	4	15.38	1	3.57	2	2.94	0	0.00	7	5.11
Number	26		28		68		15		137	
** Some participants used more than one type of drug prior to heroin.										
2.3) Route of administration										
Intravenous	4	15.38	1	3.57	8	11.76	4	26.67	17	12.41
Snorting	1	3.85	0	0.00	41	60.29	6	40.00	48	35.04
Smoking	21	80.77	27	96.43	19	27.94	5	33.33	72	52.55
Total	26	100.00	28	100.00	68	100.00	15	100.00	137	100.00
2.4) Reasons for first heroin use										
Peer pressure	7	26.92	12	42.86	14	20.59	2	13.33	35	25.55
Curiosity	17	65.38	13	46.43	51	75.00	12	80.00	93	67.88
Enjoyment	0	0.00	0	0.00	1	1.47	0	0.00	1	0.73
Coping problems/										
reducing stress	1	3.85	3	10.71	1	1.47	1	6.67	6	4.38
Others	1	3.85	0	0.00	1	1.47	0	0.00	2	1.46
Total	26	100.00	28	100.00	68	100.00	15	100.00	137	100.00

In-depth interviews revealed intriguing insights into the initial use of heroin among the case studies. These reasons were not merely immediate but often linked to underlying factors, such as family dynamics or influences from close individuals, including parents or siblings, which contributed to their decision to use heroin. In some cases, the influence of peers, combined with curiosity and the availability of drugs, played a significant role, as reflected in the following examples.

"I saw my grandmother smoking heroin since I was a child. She forced me to smoke it when I was 10 years old and even taught me how to do it. So, I smoked it following her lead. After smoking, I felt drowsy, coughed, got intoxicated, and fell asleep."

"I wanted to try it myself. I saw my uncle smoking it, so I pooled money with friends to buy heroin and smoke it. The first time I tried, I coughed, felt dizzy, drowsy, and nauseous."

"I used it because I was stressed about family issues with my wife and kids. I had seen my friends use it before, so I wanted to try it to relieve stress and relax. I inhaled it once and felt a bitter taste in my throat, dizziness, irritation, and a burning sensation in my nose."

"At first, I thought it was ketamine, so I asked my friend to try it. But my friend said it wasn't ketamine; it was heroin. I didn't know what heroin was, so I wanted to try it out of curiosity."

"A friend invited me to try it, saying that heroin wouldn't show up as a positive result in urine tests. I was already a bit drunk and in the mood, so I tried it. My friend said it was good, and I wanted to experience it myself."

Heroin use in combination with other substances; this study found that heroin users could be categorized into two groups: 1) Exclusive heroin users: approximately 59% of users reported using only heroin. 2) Heroin use with other substances: The remaining group used heroin alongside other substances, including smoking heroin with cigarettes (around 25%), combining heroin with methamphetamine (8.76%), mixing heroin with cannabis (1.46%), and using heroin along with ketamine and/or crystal methamphetamine (1.46%).

Regarding the sources of heroin, qualitative data revealed two primary means by which users obtained it. 1) Purchasing: Users often bought heroin from friends, acquaintances, drug dealers, or couriers within their community or nearby villages. 2) Receiving Without Payment: In some cases, heroin was obtained through non-monetary means, such as being given by friends, working in exchange for it, or acting as a drug retailer.

"I bought heroin from friends in the same village, people I already knew. It costs 100 baht per coffee straw." (One straw is about the length of a fingertip and can be used approximately twice.)

"I bought it from a friend in the village: one 'big' costs 700 baht, and one 'cap' costs 200 baht."

"I bought it from a Lahu hill tribe. A friend recommended this seller who lives in a nearby village, though sometimes they come to sell in our village. The price is 200 baht per cap."

"I had a friend buy it for me or bought it directly from my friend for 500 baht per gram."

"I bought it from someone in my neighborhood, recommended by a friend. At first, I had my friend buy it for me, but later, I started buying it myself. The price is 200 baht per straw."

3.2) Related Behaviors

O Drug Overdose

Among the respondents, 14 out of 137 individuals (10.22%) reported having experienced a heroin overdose. The primary cause was resuming heroin use after a period of abstinence.

"At that time, I had just been released from prison. I craved it badly and used more than usual, overdosing. I blacked out, but luckily, an elder saw me and took me to the hospital."

"One time in 2020, I blacked out in the bathroom and lost consciousness. When I woke up, I was on a bed, and my older brother had probably saved me."

"It happened around 2021. I injected too much heroin because sniffing it didn't make me high. I injected a large amount, went into shock, and passed out. No one saw me because I was alone. When I woke up, the needle was still in my arm. I later learned that the way to recover is to sweat a lot and inject saline solution, which helps alleviate the symptoms."

When asked whether they had ever witnessed someone overdosing on heroin, 23 respondents (16.79%) stated that they had seen friends or acquaintances experience a heroin overdose.

"In 2019, I was using heroin with a friend, but my friend went into shock and passed out. I let him sleep for several hours. When he regained consciousness, I gave him water to drink and some food to eat."

"About a year ago, I saw it happen, but my friend passed away. He died with the needle still in his arm."

"I've seen two people overdose together. One of them died with the needle still in their arm, while the other was saved after being taken to the hospital in time."

O Drug Dependence Treatment

Regarding the treatment of drug dependence, it was found that among the 137 respondents, who were heroin addicts aged 12 to 25, approximately half of the respondents, or 50.36%, had never undergone treatment. Those who had received drug treatment were divided into heroin treatment at 42.34%, methamphetamine at 5.11%, and the rest were treated for other substances. Qualitative data:

"I had undergone treatment once at Maeai hospital. I stopped for about 3 months. I had gone to treatment because my parents forced me to. I didn't want to quit. After completing the treatment, I got back to being dependent again because I felt the urge to."

"I had been through treatment twice, but I returned to depend on it every time I wanted to and thought I couldn't quit."

*"Yes, the first time I was being treated at the Public Health Service Center 41 (Klong Toey), the therapy did*n't work, so I went cold turkey myself, and it took a month to recover. But eventually, I surrendered because I had a fight with my brother, and I craved it. The last time my

treatment was arranged at the Public Health Service Center 41 (Klong Toey), I went cold turkey myself, and it hadn't even been a week."

"Yes, I went through drug treatment at a hospital with traditional Thai medicine. They prescribed me cannabis oil, which allowed me to stop using heroin for 5 hours a day."

3.3) Consequence

o Health Effects

When inquiring about health condition after being dependent on heroin, compared to prior to an addiction, it was found that 36.50% reported heroin addiction made their bodies weak and fatigued, while another 27.01% indicated that it made their bodies thin and emaciated. Remarkably, around 1/4 stated that heroin dependence did not cause any changes to their physical bodies.

When asked about emotions and thoughts, 36.50% of respondents reported that there had been no changes in their emotions and thoughts before being addicted to heroin. Meanwhile, some reported information indicating both negative and positive effects in which. The negative effects included irritability, impatience, and short-tempered (34.31%); no desire to meet or speak to anyone (6.57%); and being caused anxiety (2.19%). While the positive effects were less frequent, for example, being in a good mood and having a sharp mind (8.76%).

o Social Impact

Out of 75 case study participants, 54.74% believed that their dependence on heroin does not cause other people any harm or they were being indifferent to what others thought of being harmful. Meanwhile, 51 people (37.23%) perceived that their heroin addiction causes issues with their parents or family members, and another 11 people (8.03%) considered that their heroin use disorder caused the community to despise them or led to conflicts with neighboring communities.

For the in-depth information, the respondents provided opinions on the impact to family and community due to heroin abuse as follows:

"It caused trouble and led to family separation. I live in a police flat, and people perceived my family in a bad way because we have children who are addicted to drugs. As a result, I had quarrels and argued with my family."

"I frequently argued with my family because they can't accept that I, as their child, am dependent on drugs."

"I didn't cause any trouble for anyone, but society and community disdained me."

"I thought it doesn't bother anyone because using (substances) doesn't cause trouble to anyone. I smoke only at home, and my family doesn't mind or scold me."

"My family was worried and wanted me to stop, but the community wasn't affected because I smoke my own and didn't bother anyone."

4) Abstaining Heroin

The majority of this group, 91.97%, would prefer to stop using heroin. Those who do not yet desire to quit, overall 11 people (8.03%). The reasons for not being willing to stop using heroin were various. Some of them were being indulged in the taste, while others said that the environment triggered them not to quit.

Regarding the question, "Who can help to quit being dependent on heroin?" it was found that about half of the respondents believed that their parents could help them quit. The second most common answer was getting a treatment (doctors/nurses).

Conclusion and Recommendation

From the National Narcotics Treatment and Rehabilitation Data System, from 2017 to 2023, it was found that the number of heroin treatment cases has been continuously increasing, particularly among juveniles. This study selected samples from provinces with a high number of adolescents undergoing treatment, gathering data within communities and specifically interviewing young heroin dependents to observe the epidemic of heroin. The results show that the younger generation tries heroin out of curiosity and peer pressure, and often starts at a young age. Most use smoking and/or inhaling methods, with fewer using injections. However, some have already experienced overdoses. Regarding the impacts of heroin use disorder, most of them believe that their drug dependence is not considered harmful to communities. In terms of health, some regarded heroin as a substance that causes fatigue and irritability, and the majority are willing to quit, thinking that their parents and family members can help them. These findings should be adequate to set preventive programs against heroin dependence among juveniles. For those who have already been dependent on heroin, knowledge cultivation and useful advice to quit, along with family members, especially their parents, playing an essential part during the process of the treatment, or assisting them to successfully abstain.

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Discovering the Problems and Identifying Preventive Solutions for Heroin Use Among Children and Youth in the Western Region of Thailand

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Abstract

The objective of this research was to examine the problems associated with heroin use among youth in the western region of Thailand and to develop preventive guidelines. A mixed-methods approach was employed, combining quantitative and qualitative methods. The quantitative component involved a questionnaire with an Index of Congruence (IOC) ranging from 0.60 to 1.00, administered to 205 youths aged 15 - 24 years with prior heroin use, residing in Kanchanaburi, Ratchaburi, Nakhon Pathom, and Suphanburi provinces. Purposive sampling was used, and the data were analyzed using descriptive statistics, including mean, standard deviation (SD), frequency, and percentage. The qualitative component utilized semi-structured interviews with an IOC of 0.60 - 1.00, involving 31 youths with heroin use experience, 18 parents, 11 narcotic therapy officers, and 14 community leaders engaged in the community therapy project. Content analysis was employed to interpret qualitative data.

The quantitative results revealed that 92.2% of the participants with heroin use had previously smoked cigarettes. The average age at first heroin use was 18 years (range: 13 - 23). At the time of their first use, most participants (69.3%) smoked heroin mixed with cigarettes or tobacco. When categorizing by age groups, smoking heroin mixed with cigarettes was the most common method across all groups, followed by using heroin alone and heroin mixed with cannabis, respectively. Participants reported that they first received heroin primarily from friends (79.7%), followed by community members (9.9%) and family members (2.0%). Regarding the effects of heroin use, the most commonly reported issue was cravings or withdrawal symptoms (73.7%), followed by financial problems (68.3%) and health problems (63.9%), respectively.

The qualitative results revealed that participants began using heroin between the ages of 13 and 23, with a history of prior drug use. Most youths reported that their heroin use was influenced by friends and family members, coupled with a lack of knowledge and understanding about narcotics, unawareness of the consequences, and a desire for social acceptance. They described heroin as inducing feelings of happiness, absent-mindedness, and relaxation. Participants also noted significant effects of heroin use on their physical and mental health, work efficiency, finances, and relationships with family members and others. Regarding the legal consequences, these youths were rejected by society, causing negative effects on the communities they lived in. In terms of prevention, there is a critical need for knowledge dissemination about the consequences of heroin use among children, youths, parents, and other stakeholders. For therapy, participants emphasized that willingness to undergo treatment should be the primary consideration, supported by environmental improvements and care from family members and society to ensure successful treatment and rehabilitation.

Key words: Heroin, Narcotic Use Behavior, Youth

Introduction

According to the 2019 National Household Survey on Substance Use, 309 out of 100,000 people aged 12 - 65 years had experience with opium, with the highest prevalence in Bangkok and the Northern region. Additionally, 383 out of 100,000 people had experience with heroin, with the highest concentration in Bangkok, the Northern, Southern, and Central regions. Notably, the heroin user rate in the Central region was five times higher than opium use, while in the Southern region, it was ten times higher (Manop Kanato et al. 2019). Furthermore, the ASEAN Drug Monitoring Report 2022 (Manop Kanato, Rachanikorn Sarasiri, Poonrut Leyatikul. Eds., 2023) highlighted that heroin-related arrests in Thailand significantly increased between 2018 and 2022, rising from 1,061 kilograms to 3,370 kilograms, before decreasing to 848 kilograms in 2022. However, heroin has still been detected as an ingredient in the popular synthetic drug among teenagers known as "Happy Water," which contains a mix of psychoactive substances such as heroin, ecstasy, ketamine, methamphetamine, and caffeine.

Moreover, the report of the heroin epidemic situation in narcotic therapy from fiscal years 2019 - 2022 (National Addiction Treatment & Rehabilitation Committee data, as evaluated by the Office of the Narcotics Control Board (ONCB) on 10 May 2023) indicated a continuous increase in heroin patients in the western region. Cases rose from 23 in fiscal year 2019 to 445 in fiscal year 2022, with the majority being male. When classified by age, the number of patients aged 12-17 years increased from 6 cases in fiscal year 2019 to 43 cases in fiscal year 2022. Among those aged 18-24 years, cases rose significantly from 9 to 234, accounting for 62% of heroin treatment patients in fiscal year 2022. In the first half of fiscal year 2023, data revealed that 45.36% of heroin treatment patients were children and youths under 25 years of age seeking treatment for the first time. Most began using heroin between the ages of 15-19 years (63.86%), followed by those under 15 years (28.71%). The most common method of use was smoking (78.88%), followed by sniffing (12.75%) and injection (8.37%).

Additionally, there were behaviours involving the use of heroin mixed with cannabis by sprinkling heroin on cannabis and smoking it. Notably, 30% of youths in the western region accounted for the country's overall youth heroin treatment cases, with 19% originating from Kanchanaburi Province, followed by Ratchaburi, Prachuap Khiri Khan, Suphanburi, and Nakhon Pathom provinces, respectively.

As mentioned earlier regarding demand and supply data, it was found that the statistics of heroin-related arrests have been increasing, paralleling the rise in the number of treatment patients, especially among youths in the western region. The number of youths undergoing heroin treatment in 2022 increased 20 times compared to 2019. Moreover, youths in the western region accounted for one-third of all heroin treatment patients nationwide. Hence, the researchers are interested in studying heroin usage among youth heroin users in the western region. The study focuses on heroin-using behaviours, access to heroin, and the effects of heroin use on the individuals and their families, with the aim of using this information to support efforts in addressing and preventing heroin-related issues among children and youths in the future.

Objectives

1) To examine the heroin use problems among youth heroin users in the western region, categorized as follows:

1.1) Heroin use behaviors of youth heroin users in the western region.

1.2) Access to heroin among youth heroin users in the western region.

1.3) Outcomes and effects of heroin use on youth heroin users in the western region.

2) To identify preventive solutions for addressing heroin use problems among youth heroin users in the western region.

Methodology

This study employed a mixed-method research design as follows:

1) Quantitative study: This component focused on heroin use behaviors, access to heroin, and the effects of heroin use among youth heroin users in the western region. The sample consisted of 205 youths aged 15 - 24 years who had experience using heroin and resided in the western region, namely Kanchanaburi, Ratchaburi, Nakhon Pathom, and Suphanburi provinces.

The research tool was a questionnaire consisting of 16 questions.

Data were analyzed using mean, standard deviation (SD), frequency, and percentage.

2) Qualitative study: This component aimed to explore heroin use behaviors, access to heroin, the effects of heroin use, and to identify preventive solutions for heroin-related problems. In-depth interviews were conducted with the following participants:

2.1) 31 youths selected by the researchers to provide detailed information.

2.2) 18 parents of youths with experience using heroin, residing in the western region.

2.3) 11 narcotic therapy officers working in the western region.

2.4) 14 community leaders from the western region.

The research tool was a set of in-depth questionnaires containing seven open-ended questions.

Data were analyzed through content analysis to derive conclusions, which were then integrated with the quantitative findings.

Study results

1) Quantitative results

1.1) General information of the sample group

The sample group consisted of youths aged 15 - 24 years who had experience using heroin and resided in the western region. Regarding gender, 98 percent were male and 2 percent were female. In terms of age distribution, 54.2 percent were aged 21 - 24 years, 31.2 percent were aged 18 - 20 years, and 14.6 percent were under 18 years old. Education background revealed that 73 percent of the youths had graduated from secondary school or below. Among the group, 30.7 percent were no longer in the educational system, with 30 percent having dropped out due to drug-related problems and 25 percent unable to continue their studies. The analysis of income data revealed that the lowest income reported was 0 baht, while the highest income, 30,000 baht, was earned by an individual working as a contractor.

1.2) Heroin use experience

Analysis of the sample group's drug use experiences revealed that the minimum number of drug types used by the youths was one, while the maximum was 14. Among the sample, 92.2 percent reported having experience with cigarettes, with the youngest age of initiation being 10 years old. Cannabis was the second most commonly used substance, with 80 percent reporting use, and the youngest age of initiation was 11 years old. Kratom juice cocktails were used by 57.6 percent of the group, with the youngest age of initiation being 12 years old. Most drugs were first used before the age of 15, with cocaine having the highest minimum age of first use at 17 years. Detailed data is provided in Table 1 below.

Table 1: Percentage and First-Time Use Age of Drugs Among the Sample Group

Drug Type	Amount	Percentage	First Time Using Age (Years) old)		
			Lowest	Highest	Average age
Heroin	205	100.0	13	23	18
Cigarette	189	92.2	10	20	14
Cannabis	164	80.0	11	21	15
Kratom Juice Cocktail	118	57.6	12	24	17
Alcohol	116	56.6	12	21	15
Methamphetamine	74	36.1	13	22	17
Analgesics	69	33.7	13	23	17
Cough Medicine	63	30.7	12	23	17
E-cigarette	61	29.8	12	23	16
Ketamine	35	17.1	13	23	19
CNS Depressants	29	14.1	12	22	18
ICE	21	10.2	15	23	18
Sleeping Pills	20	9.8	12	20	18
Opium	10	4.9	14	20	17
Inhalant	5	2.4	14	17	15
Ecstasy	6	2.9	14	20	17
Cocaine	2	1.0	17	20	19

The study results revealed that among the 205 youths who had experience using heroin, 94.1 percent reported having used it within the past year. Additionally, 75.1 percent had used heroin within the past 30 days, and 72.7 percent had used heroin for more than 20 days during that period. When analyzing heroin use by age group, it was found that the prevalence of current use was lower among youths under 18 years old compared to older groups. Current use was reported by 66% of those under 18, 74.5% of those aged 18 - 20, and 79.3% of those aged 21 - 24. Detailed data is presented in Table 2 below.

Table 2: Amount and Percentage of Heroin Use in the Past Year, Past 30 Days, and Days Used in the Past 30 Days, Classified by Age Group

Time Range	Under 18 Years Old		18 - 20 Years Old		21 - 24 Years Old		Total	
	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent
Ever Used	47	22.9	47	22.9	111	54.1	205	100
Used in 1 Year Ago	44	22.8 (93.6)	45	23.3 (95.7)	104	53.9 (93.7)	193	100 (94.1)
Used in 30 Days Ago	31	20.1 (66.0)	35	22.7 (74.5)	88	57.1 (79.3)	154	00.(75.1)
Used More Than 20 Days	*23*	*74.2*	*22*	*62.9*	*67*	*76.1*	*112*	*72.7*
Used 6 - 20 Days	*2*	*6.5*	*4*	*11.4*	*9*	*10.2*	*15*	*9.7*
Used 1 - 5 Days	*6*	*19.4*	*9*	*25.7*	*12*	*13.6*	*27*	*17.5*

The analysis of the age of initial heroin use revealed that the average age of first use was 18 years, with the youngest age being 13 years and the oldest 23 years. 50 percent of the sample group reported starting heroin use before the age of 18. Regarding the duration and initiation of heroin use, 22.4% of the group had been using heroin for 4 years, 21.9% for 3 years, and 18.8% for 2 years. Additionally, 8.9% of the group had been using heroin for less than 1 year. Notably, 66% of the sample group had started using heroin within the past 4 years.

The study result on heroin use revealed that 69.3 percent of the sample group initially used heroin by smoking it mixed with cigarettes or tobacco. When classified by age groups, smoking heroin mixed with cigarettes was the most common method in all age groups, followed by smoking heroin alone and smoking it mixed with cannabis. According to the sample group data, there were seven cases of first-time heroin use via blood vessel injection—two cases in the 18 - 20-year-old group and five cases in the 21 - 24-year-old group. Among those who reported using heroin within the past year, 68.4 percent primarily smoked it mixed with cigarettes or tobacco, while 36.8 percent smoked it mixed with cannabis. Additionally, the data showed that 11 cases, or 5.7 percent, involved heroin use via blood vessel injection. See the detailed table 3 below.

Table 3: Amount and Percentage of Heroin Use Methods Among Youth Heroin Users (Ever Used and Used in the Past Year)

Heroin Use Method	Ever Used (n = 205)								Used in the Past Year (n=193)	
	Under 18 Years Old		18 - 20 Years Old		21 - 24 Years Old		Total			
	n	%	n	%	n	%	n	%	n	%
Smoking with Cigarette	6	2.9	68	33.2	68	33.2	142	69.3	132	68.4
Smoking with Cannabis	3	1.5	13	6.3	20	9.8	36	17.6	71	36.8
Smoking Mixed Cigarette and Cannabis	0	0.0	3	1.5	7	3.4	10	4.9	8	4.1
Smoking Only	3	1.5	38	18.5	45	22.0	86	42.0	31	16.1
Blood Vessel Injection	0	0.0	2	1.0	5	2.4	7	3.4	11	5.7

Furthermore, the study result regarding the effects of heroin use on the sample group revealed that 73.7 percent of heroin users experienced addiction effects or withdrawal symptoms. This was followed by income-related effects at 68.3 percent and health-related effects at 63.9 percent.

2) Qualitative results

2.1) Heroin use behaviors: Interviews with youth heroin users revealed that the youngest reported age of first heroin use was 13 years, often preceded by the use of other substances such as alcohol, cigarettes, electronic cigarettes, opium, kratom, cannabis, tramadol, ketamine, ICE, methamphetamine, and inhalants. Reports from treatment teams further indicated that the youngest child enrolled in a heroin treatment program was just 8 years old. Several cases disclosed that they used heroin alongside other substances, employing various methods such as smoking, sprinkling heroin on tobacco leaves or cannabis, and rolling it into cigarettes, a method known as "Pun-Lum." Some participants reported using heroin with marijuana hookahs or through glass tubes fashioned from light bulbs. Others combined heroin with opium and betel leaves. Additionally, some individuals used heroin via blood vessel injection, mixing it with water. Participants noted that, compared to smoking, injection provided stronger effects, making them feel more relaxed and sleepier, while also saving costs and reducing the quantity of heroin needed. However, some expressed fear of injections due to their associated risks and potential dangers.

When considering the cause of heroin use, many cases reported that their initial use was influenced by invitations from friends at school or within their community, with some even citing family members as influencers. A lack of understanding about drugs, insufficient knowledge of heroin's effects, and a desire for acceptance among peers were also significant factors contributing to first-time use. After their initial use, individuals reported feeling good, happy, and experiencing relief from any physical pain. However, repeated use quickly led to addiction, with users seeking larger quantities and eventually entering a relapse stage.

2.2) Heroin access: Research participants reported that they were able to purchase heroin through friends at school and outside of school. Some cases indicated that heroin was obtained

from individuals in their community, relatives, or nearby neighbors. It was also revealed that youth heroin users were sometimes used as small-scale sellers within their communities or schools, receiving monetary benefits or discounts on their purchases in return. Some participants also reported acquiring heroin by exchanging methadone, which they received free of charge as part of heroin treatment programs. The reported exchange rate was 10 cc of methadone for 100 baht worth of heroin.

2.3) Outcomes and effects: Youth heroin users reported that their first impressions of heroin use included feelings of extreme joy, relaxation, and comfort. Some cases mentioned that heroin relieved pain from various conditions, such as gonorrhea. They also highlighted advantages of heroin compared to other drugs, such as opium, noting that heroin was easier to use and had more intense effects. Some youths stated that they preferred using heroin over cannabis due to the misconception that heroin does not harm the brain like cannabis, which they believed caused paranoia. Furthermore, they described smoking heroin mixed with cannabis as more fragrant and less bitter than smoking cannabis alone, enabling them to function and work as usual.

Heroin use affects multiple aspects of life, including physical health, mental health, work, finances, relationships, and legal status. **Physically**, heroin causes weight loss, memory impairment, bone pain during withdrawal, and sleeplessness due to drug-seeking behavior. When unable to access heroin, users resort to taking frequent showers, known as "Chon-Num," for temporary relief. **Mentally**, users often struggle with emotional instability, becoming easily irritable, with some experiencing auditory hallucinations. **Professionally**, the sedative effects of heroin heavily impair work performance, reducing productivity and self-control. Additionally, many youths reported that if they did not use heroin, they experienced severe pain that made it impossible for them to work. This led to conflicts with their supervisors, ultimately resulting in job loss. They expressed regret, stating that if they could turn back time, they would avoid getting involved with heroin or associating with those who introduced them to it. **Economically**, given that heroin is a high-cost and highly addictive substance, its use often leads to continuous consumption. Heroin users reported experiencing severe physical withdrawal symptoms when they were unable to access it. Additionally, its sedative effects impair their ability to work, leading to a loss of income. Many users accumulate debt, rely on financial support from family members, or resort to selling personal belongings. In some cases, they steal items from both their family and others to sell in order to purchase heroin. In terms of **family and community relationships**, youth heroin users reported feeling that their families viewed them differently, and their relationships with family members became distant due to a lack of shared activities. They also struggled to access heroin when traveling to other provinces. Although family members often felt sadness or disappointment upon learning about the youths' heroin use, they rarely criticized or severely punished them. Instead, families provided guidance and encouragement for the youths to enter rehabilitation programs. However, some users reported that a lack of understanding about withdrawal symptoms and the difficulty of quitting heroin negatively impacted their mental health, often leading to relapse. Additionally, there were reports of social rejection within their communities.

Once people in their surroundings became aware of their heroin use, they reacted with visible changes in behavior, such as expressions of disapproval, avoidance of eye contact, or keeping their distance. Community members often discouraged their children from interacting with youth heroin users. As a result, these youths tended to isolate themselves and associate only with other heroin users. **For legal impacts**, many youths reported being prosecuted by the police or local administrative authorities. Some were arrested following blood tests that revealed heroin use, while others were detained on charges of assault or robbery, often driven by the need for money to purchase heroin. The penalties included imprisonment and fines, depending on the severity of the charges. In some cases, youths were required to enter 15-day rehabilitation camps organized by local administrative authorities.

The effects on the parents of youth heroin users revealed that parents often expressed worry when witnessing their children's withdrawal symptoms, leading them to give money to purchase heroin to alleviate the distress. In some cases, youths displayed aggressive behavior or violent tendencies when they could not access the drug. Additionally, some parents reported the loss of valuable household items, as youth users would sell these items to fund their heroin use. Misunderstandings about the severity of heroin withdrawal and the difficulties of treatment often exacerbated family tensions.

The impact on treatment staff includes challenges such as patients withdrawing from treatment and losing contact with staff. There have been reports of staff being threatened, including inpatient nurses, pharmacists, and other patients, who were disturbed during their recovery. Additionally, there is anxiety among staff about future operations, particularly regarding patient follow-up and collaboration in community -based treatment programs. This concern is due to policy changes involving the realignment of primary care units or sub-district health promotion hospitals under the jurisdiction of local administrative organizations (Ministry of Interior), which previously worked closely with community hospitals under the Ministry of Public Health.

Furthermore, regarding the impact on the community, community leaders emphasized that a strong community relies on having quality individuals. When youths are involved with drugs, the community loses valuable resources, as some youth heroin users exhibit behaviors that disrupt community peace. Additionally, they engage in activities such as destroying or stealing community resources to sell and obtain money for heroin use.

2.4) Preventive and problem-solving measures

In terms of preventing heroin-related issues, respondents emphasized the critical need to create awareness and provide knowledge about heroin to youths, parents, and all relevant stakeholders. This education aims to raise awareness of the consequences and impacts of heroin use. Many youths reported that their initial heroin use stemmed from a lack of knowledge, often due to the various street names for heroin, such as Pae, Pang Mao, or Kai. Some stated that they started with cannabis but found it insufficient to meet their needs, leading them to seek other substances to enhance its effects. Peers or older friends often introduced them to heroin by suggesting they sprinkle "powder" onto cannabis. Many became addicted to heroin shortly after, even if they initially did not realize it was heroin or were unaware of its consequences.

Providing knowledge about heroin to youths is critically important, especially for secondary school students, as the youngest age reported for initial heroin use was just 13 years old, which is already in lower secondary school. Therefore, effective prevention efforts must target secondary school students while also raising awareness among parents and the general public about the dangers of heroin use. Additionally, providing knowledge to parents about caring for children with special needs, such as those with attention deficit hyperactivity disorder (ADHD) or learning disabilities, is crucial because inappropriate parenting approaches can negatively impact a child's mental health and potentially lead to drug dependence.

Discussion

The study on the behavior of children and youth heroin users in the western region revealed that the youngest age of heroin use was 13 years, with an average starting age of 18 years. The most common method of use involved smoking heroin mixed with tobacco rolled into cigarettes or mixed with cannabis and smoked as a joint or through a bong. Many youths stated that their first heroin use occurred without realizing that heroin was mixed into the cannabis or cigarettes they consumed. Some reported knowing only that it was called "Paeng Mao" or a powder sprinkled on cannabis to enhance its effects, making it more potent than smoking cannabis alone. Others were aware that the powder mixed with the cigarettes or cannabis was heroin but had no understanding of its severe effects, including rapid addiction and intense withdrawal symptoms, which made quitting difficult. Additionally, some youths used heroin by injecting it into their veins, explaining that this method was more economical and provided a stronger effect than smoking.

Youth in the study area reported that they primarily obtained heroin from friends, either directly or by purchasing it through them. Some also mentioned acquiring heroin from family members or individuals in their community living nearby. The inability to stop using heroin often led to financial difficulties, prompting some youths to engage in drug dealing. They would sell drugs to generate money to buy heroin, with some purchasing heroin in large quantities and reselling portions of it. In addition to selling heroin for cash, there were instances where heroin was exchanged for methadone, which the youths obtained through heroin rehabilitation programs. Reports also indicated cases of methadone being sold online.

The impacts of heroin use among youths in the western region were found to primarily affect health, including withdrawal symptoms such as severe pain, chills, and what is commonly referred to as "cold turkey" due to drug deprivation. Economic impacts were also significant, as daily heroin use became essential, making it impossible to stop and leading to illegal activities to obtain money for heroin. These activities included stealing valuables from their own homes, community members, and even public property within the village to sell for heroin funds. Beyond the direct impacts on the youths themselves, heroin use also affected their families, communities, and treatment staff, such as strained family relationships, mistrust, and social exclusion from community events or activities. Medical and rehabilitation staff faced an increasing workload and complexities in providing care. In some cases, youths undergoing rehabilitation with severe withdrawal symptoms resorted to threatening or intimidating medical staff to obtain higher doses of methadone.

To effectively prevent and address heroin use among children and youths in the western region, it is essential to start with providing fundamental knowledge about heroin. This education should target not only children and youths but also schools, parents, and communities to ensure a comprehensive understanding of the current situation, the effects, and the consequences of heroin use. Additionally, it is crucial to equip children and youths with skills in refusal, critical thinking, and self-control when faced with peer pressure or invitations to try unknown substances. This aligns with the findings of the Chiang Mai Drug Rehabilitation Center (2004), which highlighted that a lack of refusal skills, especially among peer groups, and the desire for acceptance and belonging are significant social factors contributing to substance abuse among youths.

In addition, current news tends to prioritize certain drugs over heroin, the "king of drugs," leading to a diminished awareness of its deadly effects. This care must be rooted in love, understanding, and patience, involving all stakeholders—families, communities, and society—to work together toward more effective heroin rehabilitation. It is essential to adopt an integrated approach that incorporates diverse treatment methods tailored to the specific behaviors and withdrawal symptoms of youths. Collaboration with the community is also crucial for monitoring and managing the administration of methadone when needed to alleviate withdrawal symptoms. Ensuring convenience, continuity, and close supervision from families and communities can significantly enhance treatment outcomes. Moreover, providing acceptance, opportunities, and a vision for a positive future can help youths focus on life goals and successfully move forward.

Recommendations

1) Regarding prevention of heroin use among children and youths, relevant institutions should develop and disseminate knowledge, understanding, and awareness about heroin in all its dimensions, including its appearance, street names, and the effects of its use. These efforts should target children, youths, parents, educational institutions, communities, and the general public. This approach is essential to foster awareness of the dangers and impacts of heroin use on users, their families, and their communities.

2) Regarding enforcement and suppression efforts, due to the small packaging of heroin for retail and the development of capsule-like forms resembling general medicine, it becomes challenging to investigate and make arrests. To address this, law enforcement should utilize location-based intelligence and collaborate with the community to improve investigation and suppression efforts.

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Acute and Chronic Toxicity Studies of the Standardized Kratom Leaves Aqueous Extract in Sprague-Dawley Rats

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Abstract

Mitragyna speciosa Korth (MS), or kratom, has long been used by labourers in Thailand to boost physical energy and to reduce fatigue. Pharmacological effects of kratom leaf extract and its major indole alkaloid, mitragynine (MG), have been reported to have stimulant-like effects at lower doses, while higher doses have opioid-like effects. Its toxicological profile, however, is limited. Although kratom has been removed from the list of controlled narcotics, the use of kratom for the production of food and beverages is still under the control of the Thai FDA. The permitted level of MG in kratom products is too restrictive to make viable food and other health products. In order to establish an appropriate acceptable daily intake (ADI) of MG, with no identified risks to consumer health, toxicity studies of standardized kratom leaf aqueous extract in laboratory animals under the principles of Good Laboratory Practice (GLP) are required. This study, therefore, aimed to conduct the acute and chronic oral toxicity studies of the test item, the standardized kratom leaf aqueous extract in Sprague-Dawley (Jcl: SD), according to OECD test guidelines No. 423 and 452, respectively.

Based on an acute toxicity study, the test item at the dose of 2,000 mg/kg BW did not cause any acute toxicity and mortality in rats. From the chronic toxicity study, the tested rats were orally administered with standardized kratom leaf aqueous extract that contained MG 0.35, 1.74, and 5.21

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mg/kg BW, which were equivalent to human ADI of MG 0.2, 1.0, and 3.0 mg./day, respectively. All rats showed no abnormal clinical signs after daily oral administration of the test item for 90 or 180 days. There was no significant alteration in body weight, physical signs, symptoms, hematological and biochemical parameters in blood, and body organ weights compared to those of the control group. Although hepatocyte hypertrophy and fatty changes were observed in a dose-dependent manner in the liver of rats treated with the test item, these changes were reversible after cessation of kratom intake and were considered as non-adverse effects.

In summary, the result indicates that the oral administration of standardized kratom leaf aqueous extract contains MG 5.21 mg/kg BW (equivalent to ADI in human of 3 mg./day) is the maximum dose that can be consumed daily without affecting the physical health of normal people.

Keyword: Standardized kratom leaf aqueous extract, Acute oral toxicity, Chronic oral toxicity, OECD Test guidelines.

Introduction

Kratom is a plant in the Rubiaceae family, scientifically named Mitragyna speciosa (Korth.) Havil. It is commonly known as kratom, or thom in Thailand and ketum or biak-biak in Malaysia. Kratom is an indigenous medicinal plant of Southeast Asia used as a traditional medicine for a variety of illnesses, including coughs, fever, diarrhea, high blood pressure, malaria, worm infections, and muscular soreness (Suwanlert S.; 1975). Natives, especially farmers and labourers, consume kratom by chewing its fresh leaves, drinking kratom tea, or smoking kratom to increase endurance and their work productivity while working under the heat of the sun. Besides the health benefits of kratom for pain relief and increased energy, its recreational drug effects also cause a widespread increase in the use of kratom or kratom-based products. So far, many farmers in Thailand have grown substantial amounts of kratom trees after the kratom plant was legalized and promoted as an economically viable agricultural product, as it could be developed into pharmaceutical products, dietary supplements, or food additives in conventional food.

Kratom leaves are known to contain active ingredients, namely mitragynine (MG) and 7-hydroxymitragynine (7-OHMG). These two active ingredients have analgesic or pain-relieving effects. Additionally, MG has the potential to cause addiction, similar to narcotics but less addictive. Therefore, it has been proposed to be used as a substitute medicinal product for treating morphine addicts (Sabetghadam A et al., 2013). There are more than 50 alkaloids, of which MG and 7-OHMG are the main psychoactive alkaloids that have opium-like effects by acting on μ-, δ-, and κ-opioid receptors in the brain. This compound also interacts with other receptors, such as adrenergic and serotonergic receptors and neuronal $Ca2^{+}$ channels in the central nervous system, to have its neuropharmacological effects (Kerrigan S and Basiliere, 2022; Hossain R et al., 2023; Annuar NAK et al., 2024).

For the safety study of this plant, an acute toxicity study of standardized MS aqueous extract in SD rats based on the up-and-down procedure (OECD 425) reported no death, but fatigue and sleep signs were observed in male rats while only fatigue was observed in female rats. A significant decrease of mean corpuscular hemoglobin concentration (MCHC) was observed in female rats treated with higher doses (500 and 2,000 mg/kg).

Histopathology results showed centrilobular necrosis in several parts of the livers in male rats that received 2,000 mg/kg of standardized MS aqueous extract. Since there was no death after kratom treatment, it can be concluded that the LD50 value, or the amount of extract administered to test animals in a single dose that causes 50% (half) of the test animals to die, is greater than 2,000 mg/kg (Kamal MSA, et al., 2012).

Several toxicity studies have been conducted to investigate the side effects of long-term kratom use. In a subchronic oral toxicity study in the SD rats, MG toxicities were observed in the liver, brain, and kidney when these rats received pure compound of MG at the dose of 100 mg/kg BW for 28 consecutive days. Nevertheless, rats that received MG at the lower doses (1-10 mg/kg BW) showed no toxic effects, as no significant biochemical, hematological, or histopathological changes were observed after treatment (Sabetghadam A et al., 2013). In another subchronic oral toxicity study, SD rats in the tested groups were given a standardized methanolic extract of MS via the oral route at the doses of 100, 200, and 500 mg/kg BW for 28 days, and the control group received distilled water. The tested rats showed noticeable changes in body weight, behavior, and organs, especially levels of aspartate aminotransferase (AST), total bilirubin, and glucose. Moreover, based on histopathological evaluation, the standardized methanolic extract of MS was primarily toxic to the liver, lungs, and kidneys when given at doses of 200 and 500 mg/kg BW (Ilmie MU et al., 2015). It is important to note that this study used methanol to extract kratom, and methanol is classified as a toxic substance.

Recently, both acute and sub-chronic oral toxicities of kratom leaf aqueous extract were tested in Wistar rats. A single dose of the extract, either 300 or 2,000 mg/kg BW, was given to the rats according to OECD TG 423. No acute toxicity and mortality were observed during the 14-day period in an acute oral toxicity study. For the subchronic study, the extract at the doses of 250, 500, or 1,000 mg/kg BW was given to the rats daily for a total of 90 days, in accordance with the OECD TG 408 guidelines. No mortality was observed, and the obtained results showed no significant changes in body weight, food and water consumption, hematological and clinical biochemistry, relative organ weight, and histopathological effects. Compared to the control group, the findings indicate that the No-Observed-Adverse-Effect Level (NOAEL) of the kratom extract is 1,000 mg/kg body weight (Srimangkornkaew P et al., 2024). It should be noted that the MG content in the extract used in the studies was 1,822.84 mg/kg.

Furthermore, the chronic toxicity study of ethanolic kratom extract from the Department of Medical Sciences Ministry of Public Health team found that the kratom ethanolic extract at concentrations of 5, 50, 250, and 500 mg/kg BW had no adverse effects on animal body weight, food and water consumption, clinical signs, relative organ weight, and hematology of blood. However, blood chemistry levels were changed in rats that received 500 mg/kg BW of kratom leaf ethanolic extract. Significant changes in histopathology were observed in the organs of rats receiving high doses of extracts of 50, 250, and 500 mg/kg BW. Therefore, this study concluded that the minimum concentration of kratom leaf ethanolic extract in non-toxic ethanol was 5 mg/kg/day (data not published). Based on this chronic study, the Thai FDA has issued the human acceptable daily intake (ADI) of MG 0.2 mg/day. Nevertheless, this amount of MG is considered too low to produce any beneficial

effects. Previous studies showed the effective dose of MG for an antinociceptive effect in mice was 35 mg/kg B.W. (Shamima AR et al., 2012), and the ED50 of MG was 21.96 mg/kg, when assessing the dose-response relationship by utilizing the hot plate test in mice (Sabetghadam A., et al., 2013).

So far, there is no published chronic oral toxicity data of kratom extract. Therefore, this study aimed to evaluate both acute and chronic toxicities in Jcl:SD rats for a better understanding of kratom's safety profile. The results of acute and chronic toxicities of the standardized kratom leaf aqueous extract could be used as safety data for further development of kratom leaf extracts for food additives or other related products.

Objectives

This study was performed in a Good Laboratory Practices (GLP) certified test facility to investigate the acute and chronic oral toxicities of standardized kratom leaf aqueous extract in Jcl:SD rats. The extract contained MG of 0.35, 1.74, and 5.21 mg/kg body weight, which are equivalent to human ADI of MG 0.2, 1.0, and 3.0 mg/day, respectively. The objective was to determine the maximum dose of MG in kratom that could be consumed per day.

Materials and Methods

Preparation of Standardized Kratom Leaf Aqueous Extract

The standardized kratom leaf aqueous extract was provided by the GMP-certified herbal extract factory of the Medical Science Research and Innovation Institute, Research Department of Prince of Songkla University, which provided the certificate of analysis (CoA). In brief, fresh kratom leaves were collected from local farmers who adhered to Good Agricultural Practices (GAP) in Surat Thani Province. The kratom leaves were cut using an herb shredder and thoroughly washed with reverse osmosis (RO) water to remove the dirt impurities.

The wet-washed leaves were then spun using a centrifuge before dried in an oven at a temperature of 60 - 80 °C for 3 hours. The dried kratom leaves were sampled to ensure that the quantities of key substances, germs, heavy metals, and pesticides were within acceptable limits. The dried kratom leaves were put into the extractor, which was set at 140 - 160 °C under a pressure of 2-4 bars, using RO water as the solvent. The first 20 liters of extracted water were collected, cooled to room temperature, and processed into a freeze-dried powder using a freeze dryer. The kratom powder was then screened for MG content using an in-house method based on Journal of AOAC International Vol.100, No. 1, 2017, employing high-performance liquid chromatography (HPLC) technique and microbial contamination according to British Pharmacopoeias, 2020 Volume I-V. The content of MG was analyzed from lot No. WF002310123 and lot No. WF005190423 using the in-house method TM-L08 based on Forensic Toxicol., Vol.35, 2017, and was 28.93 mg/g and 37.95 mg/g, respectively.

Animals

For an acute oral toxicity study, the experimental protocol was set according to OECD TG 423 (OECD; 2001) and was approved by the Naresuan University Animal Ethics Committee (NUACUC) (NU-TS650402-19) with an approval number of 66 01 023. For a chronic oral toxicity study, the experimental protocol was set according to OECD TG 452 (OECD; 2008) and was aproved by the NUACUC (NU-TS650805-01) with an approval number of 66 01 001.

Sprague-Dawley (Jcl: SD) female rats, aged 8 weeks, were obtained from the M-CLEA Bioresource Co., Ltd., and Nomura Siam International Co. Ltd., accompanied by animal health certificate. The animals were quarantined in the quarantine room for a minimum of 5 days and acclimatized to animal room conditions for at least 7 days prior to the commencement of the study. All rats were housed in the animal holding room, which was controlled by the humidity ventilation air conditioning control (HVAC) system to maintain the following parameters: a temperature range of 22 ± 3°C, a relative humidity range of 30-70%, and a 12-hr light/12-hr dark cycle. Rats were fed with sterile rodent pellets (G082), and reverse osmosis (RO) water was available ad libitum throughout the study period.

Test Method

For an acute oral toxicity study, the first 3 rats were fasted overnight prior to a single-dose oral administration of standardized kratom leaf aqueous extract at a dose level of 2,000 mg/kg BW and continued fasting for another 3 hours after administration. All 3 rats were observed within 4 hours after administration and at least once daily for 14 days. Following no observed mortality in the first 3 rats, another 3 rats were administered orally with the same dose level of the test item. The body weight of each rat and their food and water consumption were recorded on days 0, 7, and 14 after administration. After clinical observation for 14 days, rats were sacrificed through euthanasia, and gross pathological changes were recorded. An assessment of toxicity was based on abnormal clinical signs, mortality and moribundity, body weight, food and water consumption, and necropsy findings.

For a chronic oral toxicity study, rats were divided into 3 main groups according to the administration period: A) An interim kill group consisting of 4 subgroups; 20 rats (10 male, 10 female rats)/subgroup receiving 3 doses of standardized kratom leaf aqueous extract (low, medium, and high) or vehicle for a total of 90 days, B) Main study group consisting of 4 subgroups; 20 rats (10 male, 10 female rats)/subgroup receiving 3 doses of standardized kratom leaf aqueous extract (low, medium, and high) or vehicle for a total of 180 days and C) Satellite group consisting of 2 subgroups; 10 rats (5 male, 5 female rats) receiving the high dose of standardized kratom leaf aqueous extract or sterile water (vehicle) daily for a total of 180 days and then without dosing during the recovery period for another 28 days prior to euthanasia to assess recovery and a return to normal conditions. During the period of administration, the rats were observed closely, each day, for signs of any toxicity.

Clinical sign observation

The clinical signs were observed individually after each administration of standardized kratom leaf aqueous extract. Mortality and morbidity were assessed at least once a day throughout the study period. Severity of the clinical signs and the date of occurrence were recorded for each animal.

Hematological Analysis

At the end of the chronic toxicity experiment, all rats were anesthetized by intraperitoneal injection of an overdose of thiopental (150 mg./kg. BW), and blood samples were collected from the posterior vena cava for hematology and blood chemistry analyses.

For a complete blood count (CBC) analysis, ≈0.25-0.5 ml. of blood sample was put into the vial containing K3 EDTA and was measured for the following parameters with a hematology analyzer (XN-1500V, Sysmex, USA); white blood cell (WBC), mean corpuscular volume (MCV), lymphocyte (LYM), mean corpuscular hemoglobulin (MCH), monocyte (MON), mean corpuscular hemoglobin concentration (MCHC), granulocyte (GRAN), red cell distribution width-CV (RDWc), percentage lymphocyte (%LYM), red cell distribution width-SD (RDWs), percentage monocyte (%MON), platelet (PLT), percentage granulocyte (%GRAN), mean platelet volume (MPV), red blood cell (RBC), plateletcrit (PCT), hemoglobin concentration (HGB), platelet distribution width-CV (PDWc), hematocrit (HCT), and platelet distribution width-SD (PDWs).

Clinical Blood Chemistry Analysis

After blood collection, the blood samples were kept at room temperature for ≈ 15-20 min until coagulation. Then these blood samples were centrifuged at 4,000 rpm for 10 min to obtain the serum samples, which were used to measure the following parameters: total protein (TP), albumin (ALB), alanine aminotransferase (ALT), alkaline phosphatase (ALP), blood urea nitrogen (BUN), creatinine (CRE), glucose (GLU), sodium (Na+), potassium (K+), and total cholesterol (TCHO) using a blood chemistry analyzer (DRI-CHEM NX600V IC, Fujifilm, Japan). Bile acids were detected by using the TBA colorimetric assay kit (Catalog No: E-BC-K181-M) according to the manufacturer's instructions.

Necropsy

At the end of the experiment, the rats in a chronic toxicity study were fasted overnight before euthanasia with an overdose of thiopental (100-200 mg./kg. BW; IP). After completion of blood collection, all rats were sacrificed by exsanguination. Euthanized rats were immediately subjected to gross observation of all tissues. The external appearance and the internal organs in the abdominal and thoracic cavities were observed, and the findings were recorded. The organs such as lymph nodes, thymus gland, spleen, bone marrow, and Peyer's patches, or bronchus-associated lymphoid tissue, as well as pivotal organs, i.e., brain, kidneys, liver, and reproductive organ, were examined, weighed, and recorded.

For tissue preservation, all collected tissues were submerged in 10% neutral buffered formalin for ≈ 24 hours before tissue processing and embedding to create paraffin-embedded specimens ready for sectioning. For histopathological examination, all tissue slides were cut 2 µm thick and stained with hematoxylin-eosin before being examined by histopathologists.

Statistical Analysis

All statistical analysis was conducted by using GraphPad Prism 9 software and the significance level was set at $P<0.05$. All data are shown in the mean ± SD. The data with normal distribution was analyzed for variance with one-way ANOVA, followed by Duncan's post hoc test. For data with unusual distribution, the variance was analyzed by the Kruskal-Wallis test followed by Dunn's post hoc test.

Test Results

Acute Oral Toxicity Test

The results showed no abnormalities after oral administration of standardized kratom leaf aqueous extract at 2,000 mg/kg bw to all 6 rats and no death was observed throughout the 14-day study period. The amount of food and

water consumption was less or more than the normal range on some days. The normal range of food intake for adult rats is ≈5-6 g/100 g.bw/day, and water intake for adults is approximately 10-12 ml/100 g.bw/day (Colby et. al., 2020). The average body weights of rats were found to be correlated with their growth rates. The necropsy examination showed no abnormal internal organs in all standardized kratom leaf aqueous extract-treated rats.

Chronic Oral Toxicity Test

Mortality and Moribundity

The results showed no death related to standardized kratom leaf aqueous extract administration, and no abnormalities or clinical signs were observed during the study period after daily oral administration for 90 or 180 days. However, some rats had porphyrin stains around the eyes, which might occur from stress responses during handling for oral gavage. These changes were not considered as the adverse effects of standardized kratom leaf aqueous extract since porphyrin stains were also observed in the control groups. In addition, no toxic signs or abnormal behavior were found in each treatment group.

Food and Water Consumption and Body Weight Change

During the study, food and water consumption were measured on the test item administration date and then once a week thereafter. Weighed food and water were supplied to each cage, and the remains were measured at the same time on the next day to calculate daily consumption (g/head/day). It was found that food and water consumption of male and female rats receiving standardized kratom leaf aqueous extract at each dose was in the normal range (Colby et al., 2020) in almost every week. However, some rats had lower or higher food and water consumption than the normal range in some weeks.

The average body weights of rats in this study correlated with their growth rates. At the end of each study period, no significant differences in body weight gain were observed between male and female rats receiving standardized kratom leaf aqueous extract across all dosage groups. The only exception was in the interim kill group, where female rats treated with standardized kratom leaf aqueous extract for 90 days had relatively lower body weight gain compared to their respective control group (Figure 1A).

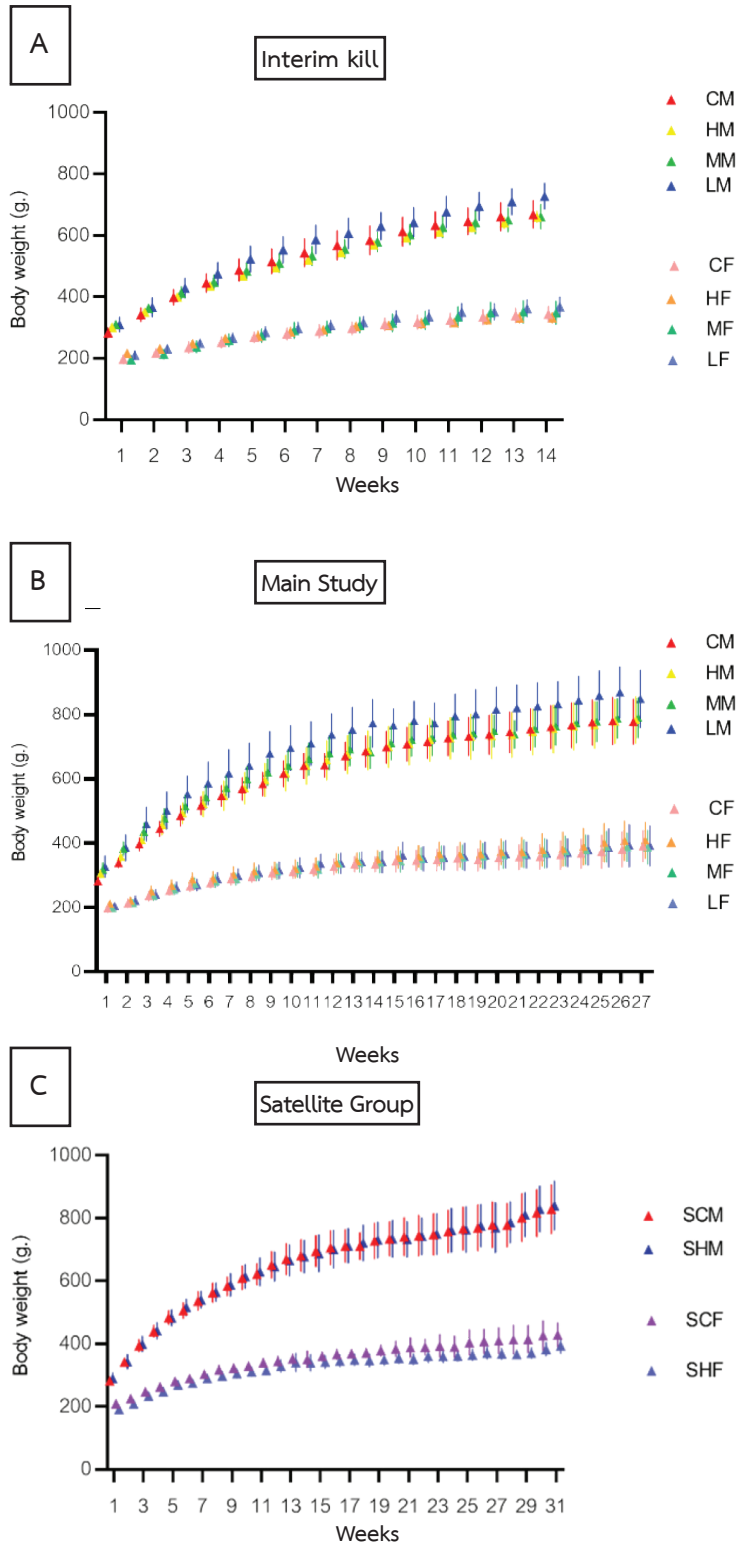

Figure 1: Body weight changes of male and female rats in the interim kill group (A), the main study group (B), and the satellite group (C) that received standardized kratom Leaf aqueous extract for 90 days, 180 days, and 180 days with a 28-day recovery period, respectively. Values are mean ± standard deviation.

Hematological Analysis

In the interim kill group, the average of MCHC in male and female rats treated with a high dose of standardized kratom leaf aqueous extract for 90 days was significantly higher than those in the control group (P<0.05). Moreover, the average of PLT and MONO of female rats treated with the high dose of the extract were significantly lower than those in the control group (P<0.05).

In the main study group, MCV and MCH of male rats treated with a high dose were significantly higher than those in the control group (P<0.05), and the average of PCT in both male and female rats that received a low dose of the extract for 180 days was significantly lower than those in the control group. No variations were observed in the hematological parameters of male and female rats in the satellite group compared to their respective control group, as shown in Tables 1 and 2.

Table 1 Hematological examinations of male rats administered with standardized kratom leaf aqueous extract for 90 days (interim kill group), 180 days (main study group), and satellite group.

PARAMETER	UNIT	INTERIM KILLS (N=10)				MAIN STUDY (N=10)				SATELLITE (N=5)	
		Control	Low	Medium	High	Control	Low	Medium	High	Control	High
WBC	10^3/µL	9.25±2.26	6.87±2.31	9.41±4.15	8.46±2.27	7.57±1.19	6.81±1.23	8.12±2.09	8.46±2.27	6.84±0.79	7.58±1.09
RBC	10^6/µL	8.86±0.32	8.96±0.48	9.17±0.59	9.30±0.58	9.17±0.47	8.87±0.29	9.00±0.39	9.45±0.75	8.50±0.22	8.92±0.18
HGB	g/dl	14.61±0.73	14.89±0.92	15.09±0.75	15.48±0.95	15.10±0.72	15.02±0.43	15.18±0.74	16.11±1.31	14.98±0.81	15.20±0.30
HCT	%	43.05±2.24	43.19±2.68	43.67±2.52	44.57±2.96	42.73±1.91	42.52±1.38	43.13±2.25	45.94±4.58	41.62±1.62	42.48±0.71
MCV	fl	48.60±1.25	48.19±1.43	47.65±1.16	47.94±0.80	46.64±1.21	47.97±1.48	47.93±1.11	48.53±1.40*	48.96±1.20	47.60±0.19
MCH	Pg	16.50±0.46	16.62±0.47	16.45±0.53	16.66±0.41	16.47±0.46	16.96±0.48	16.88±0.49	17.04±0.52*	17.62±0.73	17.04±0.09
MCHC	g/dl	33.95±0.49	34.48±0.58	34.57±0.55	34.76±0.49*	35.33±0.29	35.32±0.59	35.22±0.87	35.12±0.83	35.98±0.62	35.76±0.18
PLT	10^3/ µL	1024.20±146.32	1035.20±93.66	921.30±219.89	1024.70±157.95	896.60±95.83	861.80±94.75	864.70±124.81	979.00±152.29	859.20±36.17	771.20±111.42
PCT	%	0.71±0.08	0.75±0.08	0.66±0.20	0.74±0.12	0.76±0.07	0.67±0.06*	0.73±0.11	0.77±0.13	0.69±0.08	0.66±0.05
NEUT	10^3/µL	1.37±0.26	1.05±0.32	1.13±0.29	1.12±0.38	1.28±0.32	1.22±0.69	1.35±0.55	1.57±0.38	1.39±0.38	1.12±0.14
LYMPH	10^3/µL	7.03±2.09	5.20±2.04	7.35±3.61	6.49±1.84	5.45±1.13	4.88±0.72	7.32±3.63	5.85±1.25	4.62±0.49	5.65±1.03
MONO	10^3/µL	0.67±0.21	0.48±0.20	0.74±0.36	0.65±0.26	0.66±0.16	0.54±0.13	0.73±0.37	0.99±0.42	0.67±0.06	0.64±0.17
EO	10^3/µL	0.18±0.03	0.14±0.04	0.17±0.05	0.18±0.05	0.16±0.03	0.15±0.05	0.18±0.05	0.23±0.08	0.15±0.03	0.17±0.04
BASO	10^3/µL	0.01±0.01	0.01±0.01	0.02±0.01	0.02±0.01	0.01±0.01	0.01±0.01	0.02±0.03	0.02±0.02	0.01±0.00	0.01±0.00

Note Values are mean ± standard deviation.
*The average is statistically significant difference from the control group (P<0.05).

Table 2 Hematological examinations of female rats administered with standardized kratom Leaf aqueous extract for 90 days (interim kill group), 180 days (main study group), and satellite group

PARAMETER	UNIT	INTERIM KILLS (N=10)				MAIN STUDY (N=10)				SATELLITE (N=5)	
		Control	Low	Medium	High	Control	Low	Medium	High	Control	High
WBC	10^3/µL	4.63±1.53	5.18±1.82	3.99±1.60	5.37±1.79	7.57±1.19	6.81±1.23	8.12±2.09	8.46±2.27	3.90±1.71	3.28±0.64
RBC	10^6/µL	8.48±0.37	8.28±0.35	8.25±0.29	8.44±0.49	9.17±0.47	8.87±0.29	9.00±0.39	9.45±0.75	8.12±0.29	8.18±0.41
HGB	g/dl	14.64±0.90	14.43±0.53	14.43±0.38	14.85±1.04	15.10±0.72	15.02±0.43	15.18±0.74	16.11±1.31	14.74±0.86	14.84±0.76
HCT	%	42.77±2.94	41.91±1.53	41.27±1.53	42.43±3.18	42.73±1.91	42.52±1.38	43.13±2.25	45.94±4.58	40.96±2.93	40.74±2.11
MCV	fl	50.43±1.88	49.47±1.94	50.01±1.06	50.26±2.43	46.64±1.21	47.97±1.48	47.93±1.11	48.53±1.40*	50.36±2.41	49.79±0.54
MCH	Pg	17.26±0.56	17.47±0.94	17.48±0.50	17.59±0.81	16.47±0.46	16.96±0.48	16.88±0.49	17.04±0.52*	18.14±0.68	18.14±0.33
MCHC	g/dl	34.27±0.56	35.29±0.95*	34.96±0.63	35.00±0.29*	35.33±0.29	35.32±0.59	35.22±0.87	35.12±0.83	36.06±0.79	36.44±0.70
PLT	%	1056.70±66.10	968.20±203.60	909.40±108.90*	1009.40±90.11	896.60±95.83	861.80±94.75	864.70±124.81	979.00±152.29	841.40±88.46	862.00±55.13
PCT	%	0.74±0.07	0.68±0.14	0.64±0.09	0.68±0.10	0.76±0.07	0.67±0.06*	0.73±0.11	0.77±0.13	0.64±0.05	0.72±0.08
NEUT	10^3/µL	0.60±0.22	0.48±0.13	0.51±0.16	0.50±0.25	1.28±0.32	1.22±0.69	1.35±0.55	1.57±0.38	0.58±0.29	0.58±0.17
LYMPH	10^3/µL	3.40±1.24	4.19±1.60	3.12±1.37	4.34±1.45	5.45±1.13	4.88±0.72	7.32±3.63	5.85±1.25	2.80±1.37	2.21±0.54
MONO	10^3/µL	0.52±0.24	0.39±0.17	0.24±0.10*	0.42±0.26	0.66±0.16	0.54±0.13	0.73±0.37	0.99±0.42	0.40±0.19	0.37±0.10
EO	10^3/µL	0.10±0.04	0.11±0.04	0.12±0.05	0.11±0.04	0.16±0.03	0.15±0.05	0.18±0.05	0.23±0.08	0.10±0.04	0.11±0.03
BASO	10^3/µL	0.02±0.01	0.01±0.01	0.01±0.01	0.01±0.01	0.01±0.01	0.01±0.01	0.02±0.03	0.02±0.02	0.01±0.01	0.01±0.01

Note Values are mean ± standard deviation.
*The average is statistically significant difference from the control group (P<0.05).

Clinical Blood Chemistry Analysis

Clinical blood chemistry examination was performed in order to evaluate any toxic effects on the pancreas function (glucose), kidney function (BUN, creatinine), and liver function (total protein, albumin, total and direct bilirubin, AST, ALT, and ALP) as stated in the OECD TG 452 guidelines.

For the interim kill group, male rats receiving a high dose of standardized kratom leaf aqueous extract for 90 days had significantly higher BUN, while the level of ALT was significantly lower than those in the control group (P<0.05), as shown in Table 3. Female rats receiving a medium dose of extract for 90 days had significantly lower levels of ALT, TP, and glucose than those in the control group (P<0.05) (Table 4).

For the main study group, the average values of Cl- in male rats receiving standardized kratom leaf aqueous extract at all doses for 180 days were significantly lower than those in the control group (P<0.05). Male rats that received a high dose of extract had significantly higher creatinine, while total bilirubin was significantly lower than those in the control group (P<0.05). The level of AST in male rats that received a low dose of extract was significantly lower than in the control group (P<0.05). Female rats that received standardized kratom leaf aqueous extract at all doses for 180 days showed a significant decrease in ALP level compared to those in the control group (P<0.05). Likewise, female rats administered with a high dose of extract had significantly lower ALT levels than the control values (P<0.05). Nonetheless, all of these significant values fell within the normal ranges, and there were no variations in the blood chemistry parameters of male and female rats in the satellite group compared to the control group, as shown in Tables 3 and 4.

Table 3: Clinical blood chemistry examination of male rats administered with standardized kratom leaf aqueous extract for 90 days (interim kill group), 180 days (main study group), and satellite group

PARAMETER	UNIT	INTERIM KILLS (N=10)				MAIN STUDY (N=10)				SATELLITE (N=5)	
		Control	Low	Medium	High	Control	Low	Medium	High	Control	High
BUN	mg/dl	14.80±2.07	19.35±1.67*	17.38±2.58*	18.44±1.71*	17.61±1.96	19.44±1.48	17.15±2.16	16.02±1.65	18.44±2.18	20.08±4.52
CRE	mg/dl	0.39±0.06	0.38±0.04	0.40±0.05	0.39±0.04	0.35±0.04	0.38±0.04	0.37±0.04	0.43±0.05*	0.37±0.01	0.40±0.07
ALP	U/l	84.40±19.73	74.60±17.97	79.80±6.55	89.70±21.14	81.00±19.51	95.60±14.99	74.70±12.69	75.00±16.87	97.20±18.54	128.00±36.39
TBIL	mg/dl	0.33±0.05	0.40±0.14	0.31±0.03	0.29±0.06	0.36±0.07	0.28±0.06	0.34±0.08	0.27±0.07*	0.26±0.05	0.28±0.04
ALT	U/l	34.80±6.61	25.70±7.41*	29.70±5.42	27.20±3.49*	42.70±24.61	61.50±49.62	31.40±8.85	33.70±12.15	56.20±28.26	47.60±6.15
AST	U/l	84.50±16.32	100.80±35.01	78.30±12.01	80.60±25.95	103.40±33.63	186.70±80.69*	144.30±41.23	84.60±24.02	182.40±119.39	138.00±20.14
TP	g/dl	4.68±0.28	4.88±0.36	4.71±0.22	4.85±0.17	4.97±0.26	5.03±0.16	4.94±0.29	5.17±0.49	4.82±0.129	4.64±0.19
ALB	g/dl	3.20±0.28	3.23±0.26	3.16±0.20	3.33±0.29	3.24±0.15	3.17±0.20	3.15±0.30	3.44±0.43	3.06±0.15	3.02±0.08
GLOB	g/dl	1.48±0.09	1.65±0.15*	1.52±0.17	1.52±0.19	1.73±0.15	1.86±0.13	1.79±0.12	1.73±0.13	1.76±0.17	1.62±0.13
GLU	mg/dl	195.70±53.17	189.50±51.45	182.90±32.80	183.40±40.37	176.30±13.09	182.60±15.47	196.20±58.43	219.00±80.65	156.40±15.69	171.20±13.05
CA	mg/dl	8.72±0.51	8.50±0.51	8.62±0.53	8.67±0.47	9.42±0.29	12.17±0.52*	12.26±0.44*	12.18±2.08*	8.44±0.29	8.46±0.29
NA	mEq/l	142.90±0.99	143.30±1.42	142.40±0.84	143.00±1.63	143.40±0.97	143.90±1.45	143.70±0.48	143.70±1.89	144.60±0.55	143.60±1.52
K	mEq/l	4.29±0.99	4.16±0.55	4.49±1.23	4.22±0.93	3.75±0.13	3.72±0.19	4.13±0.72	5.01±1.81	3.94±0.35	3.96±0.29
CL	mEq/l	96.60±1.84	95.40±1.96	96.30±1.06	95.30±1.42	98.30±1.57	96.10±1.73*	95.60±1.51*	95.80±2.25*	97.00±1.00	94.80±1.30
TCO_2	mmol/l	30.92±1.90	33.68±2.93	32.91±2.55	32.58±3.97	35.21±2.31	33.53±4.25	34.29±2.76	31.87±4.04	33.52±2.68	36.70±2.77

Note Values are mean ± standard deviation.
*The average is statistically significant difference from the control group (P<0.05).

Table 4 Clinical blood chemistry examination of female rats administered with standardized kratom leaf aqueous extract for 90 days (interim kill group), 180 days (main study group) and satellite group

PARAMETER	UNIT	INTERIM KILLS (N=10)				MAIN STUDY (N=10)				SATELLITE (N=5)	
		Control	Low	Medium	High	Control	Low	Medium	High	Control	High
BUN	mg/dl	19.59±2.57	18.04±3.89	16.54±2.22	19.42±3.18	15.97±2.14	16.74±2.79	17.45±3.28	15.97±1.78	16.04±2.36	18.54±2.83
CRE	mg/dl	0.46±0.06	0.40±0.08	0.45±0.08	0.42±0.06	0.40±0.03	0.42±0.05	0.44±0.06	0.41±0.03	0.40±0.03	0.43±0.06
ALP	U/l	68.20±23.33	43.30±10.44*	40.00±10.69*	66.10±12.81	54.10±17.95	37.70±4.69*	40.30±5.38*	37.80±10.37*	40.20±17.96	37.20±9.26
TBIL	mg/dl	0.42±0.06	0.35±0.08*	0.37±0.07	0.41±0.14	0.36±0.15	0.33±0.07	0.39±0.07	0.32±0.12	0.38±0.04	0.34±0.05
ALT	U/l	25.30±7.29	26.80±15.89	30.80±16.03	30.10±3.18	41.60±12.54	35.00±14.45	28.60±7.99	24.50±5.32*	42.60±23.65	27.00±3.61
AST	U/l	64.60±11.56	77.70±36.15	89.50±60.25	75.20±25.39	112.40±49.41	183.40±86.75	143.40±36.19	98.20±34.15	119.80±54.09	67.40±9.07
TP	g/dl	6.15±0.55	5.77±0.45	5.61±0.49*	6.05±0.44	5.81±0.51	5.92±0.37	6.13±0.42	6.25±0.32	6.26±0.55	6.48±0.46
ALB	g/dl	4.82±0.52	4.60±0.47	4.43±0.35	4.85±0.54	4.59±0.49	4.65±0.45	4.83±0.40	4.88±0.35	4.66±0.48	5.26±0.32
GLOB	g/dl	1.33±0.19	1.17±0.18	1.18±0.23	1.20±0.17	1.22±0.18	1.27±0.19	1.30±0.17	1.37±0.25	1.60±0.19	1.22±0.24
GLU	mg/dl	256.60±95.57	184.90±49.99	168.90±46.29*	203.30±42.80	163.10±16.57	159.20±18.55	168.50±42.30	158.50±29.71	181.80±52.04	183.40±17.98
CA	mg/dl	9.90±0.79	9.37±0.61	9.05±0.64	9.68±0.82	12.50±0.37	12.33±0.48	12.57±0.48	12.67±0.28	9.68±0.96	9.56±0.32
NA	mEq/l	145.00±1.49	143.80±2.04	143.40±1.71	144.10±1.85	143.10±1.37	143.10±2.08	144.10±1.60	144.00±1.05	144.00±1.00	145.40±1.52
K	mEq/l	5.05±1.44	3.96±0.94	3.98±0.75	4.37±1.20	3.49±0.26	3.68±0.32	3.85±1.04	3.75±1.02	3.88±1.25	4.28±1.21
CL	mEq/l	95.40±1.35	96.70±1.57	97.80±1.99*	96.50±2.07	97.00±1.15	95.90±2.02	96.40±1.84	96.60±2.84	94.40±1.14	95.60±1.34
TCO_2	mmol/l	30.04±4.79	33.40±2.52	29.22±2.27	30.04±2.04	32.33±2.32	32.65±3.21	32.68±3.73	33.18±3.14	34.52±2.22	33.48±4.73

Note Values are mean ± standard deviation.
*The average is statistically significant difference from the control group (P <0.05).

Relative Organ Weight and Internal Organ Abnormalities

At the end of the experiment, all rats in a chronic toxicity study were necropsied, and all organs were inspected to evaluate the persistence, delayed onset, or reversibility of toxicity. Gross findings were relevant to histopathological findings in both sexes in all groups. Grossly, red spots in the lung, redness or hemorrhage in the submandibular and mesenteric lymph nodes, lymph nodes, and petechial hemorrhage in the thymus were observed in both sexes in all groups. Enlargement was observed in the liver, thyroid gland, and pituitary gland of the high-dose-treated group in both sexes.

As shown in Tables 5 and 6, the relative organ weight of the treated and control groups showed no remarkable difference. However, enlarged livers, or hepatomegaly, were observed in ≈15% (13 rats from 88 rats) in both male and female rats that received standardized kratom leaf aqueous extract for 90 and 180 days. In the satellite group, enlarged livers were observed in 4 rats from 12 rats, both male and female, that received a high dose of standardized kratom leaf aqueous extract for 180 days with a 28-day recovery period. However, the relative average weight of these organs was not significantly different from those of the control group.

Table 5: Relative weights of important organs of male rats administered with standardized kratom leaf aqueous extract for 90 days (interim kill group), 180 days (main study group), and satellite group

PARAMETER	UNIT	INTERIM KILLS (N=10)				MAIN STUDY (N=10)				SATELLITE (N=5)	
		Control	Low	Medium	High	Control	Low	Medium	High	Control	High
Body weights	g.	14.80±2.07	19.35±1.67*	17.38±2.58*	18.44±1.71*	770.98±70.83	859.36±73.72*	768.53±64.06	763.85±69.11	807.00±78.28	830.90±79.95
Spleen	% BW	660.05±45.97	706.23±41.26	654.28±40.34	643.56±16.63	0.1225±0.0139	0.1318±0.0144	0.1330±0.0127	0.1364±0.0084*	0.1430±0.0083	0.1228±0.0162*
Liver	% BW	0.1236±0.0442	0.1320±0.0149	0.1305±0.0102	0.1310±0.0176	2.3738±0.1642	2.4833±0.1959	2.3483±0.1224	2.3715±0.1641	2.5401±0.2611	2.6563±0.2825
Right kidney	% BW	2.5274±0.1211	2.5237±0.1528	2.3762±0.1248	2.5208±0.1600	0.2242±0.0163	0.2044±0.01170	0.2351±0.0188	0.2336±0.0288	0.2413±0.0145	0.2329±0.0183
Left kidney	% BW	0.2570±0.0208	0.2549±0.0124	0.2496±0.0147	0.2574±0.0228	0.2235±0.0145	0.2184±0.0140	0.2284±0.0113	0.2293±0.0247	0.2345±0.0157	0.2403±0.0154
Thymus	% BW	0.2588±0.0188	0.2457±0.0127	0.2418±0.0164	0.2560±0.0180	0.0604±0.0148	0.0673±0.0147	0.0591±0.0167	0.0614±0.0187	0.0628±0.0205	0.0515±0.0117
Heart	% BW	0.0822±0.0161	0.0853±0.0110	0.0793±0.0166	0.0714±0.0096	0.2278±0.0226	0.2229±0.0062	0.2391±0.0189	0.2384±0.0160	0.2398±0.0216	0.2218±0.0209
Lung/trachea /esophagus	% BW	0.2525±0.0239	0.2358±0.0140	0.2470±0.0188	0.2486±0.0155	0.3925±0.330	0.3597±0.0281	0.4207±0.0486	0.4114±0.0375	0.3673±0.0419	0.3334±0.0128
Brain	% BW	0.4375±0.0420	0.4316±0.0328	0.4256±0.0374	0.4153±0.0366	0.2953±0.0289	0.2754±0.0268	0.2983±0.0278	0.2984±0.0199	0.2907±0.0255	0.2803±0.0297

Note Values are mean ± standard deviation.
*The average is statistically significant difference from the control group (P<0.05).

Table 6: Relative weights of important organs of female rats administered with standardized kratom leaf aqueous extract for 90 days (interim kill group), 180 days (main study group), and the satellite group

PARAMETER	UNIT	INTERIM KILLS (N=10)				MAIN STUDY (N=10)				SATELLITE (N=5)	
		Control	Low	Medium	High	Control	Low	Medium	High	Control	High
Body weights	g	337.55±24.03	358.35±29.01	338.64±34.66	332.39±15.92	375.41±54.69	382.06±61.05	381.04±50.40	396.25±61.97	434.08±38.53	375.44±23.22
Spleen	% BW	0.1587±0.0098	0.1773±0.0268	0.1655±0.0194	0.2239±0.1198	0.1448±0.0414	0.1555±0.0339	0.1510±0.0168	0.1696±0.0210	0.1736±0.0091	0.1662±0.0221
Liver	% BW	2.9858±0.1497	2.8263±0.0886	2.6262±0.1869*	3.0360±0.2896	2.8214±0.2139	2.6901±0.2608	2.7297±0.0919	2.9212±0.2336	2.9383±0.3431	2.8325±0.2587
Right kidney	% BW	0.2741±0.0186	0.2704±0.0230	0.2604±0.0150	0.2763±0.0299	0.2461±0.0229	0.2682±0.0364	0.2619±0.0108	0.2488±0.0140	0.2656±0.0334	0.2661±0.0216
Left kidney	% BW	0.2727±0.0204	0.2660±0.0226	0.2513±0.0216	0.2584±0.0313	0.2493±0.0270	0.2603±0.0322	0.2544±0.0131	0.2490±0.0211	0.2543±0.0292	0.2767±0.0175
Thymus	% BW	0.1028±0.0181	0.1075±0.0172	0.1107±0.0212	0.1017±0.0142	0.0781±0.0250	0.0787±0.0211	0.0876±0.0220	0.0760±0.0134	0.0912±0.0247	0.0860±0.0160
Heart	% BW	0.3016±0.0301	0.2904±0.0136	0.2732±0.0486	0.2938±0.0347	0.2899±0.0454	0.3060±0.0761	0.2951±0.0235	0.2908±0.0357	0.2862±0.0109	0.3191±.0.0286
Lung/trachea /esophagus	% BW	0.5632±0.0432	0.5835±0.0707	0.5912±0.0582	0.5929±0.0770	0.5417±0.0599	0.5560±0.0906	0.5548±0.0448	0.5301±0.0691	0.5133±0.0461	0.5467±0.0315
Brain	% BW	0.5905±0.0499	0.5799±0.0418	0.5961±0.0613	0.6085±0.0340	0.5523±0.0733	0.5539±0.2795	0.5618±0.0669	0.5362±0.0724	0.5135±0.0500	0.5546±0.0186

Note Values are mean ± standard deviation.
*The average is statistically significant difference from the control group (P<0.05).

Histopathological Examination

The histopathological examination revealed prominent findings, including hepatocyte hypertrophy and mixed microvesicular and macrovesicular fatty changes (Figure 2) across all groups in both sexes. In the interim kill group, mixed microvesicular and macrovesicular fatty changes decreased in all tested male groups, both in incidence and severity, but increased in incidence in all tested female groups compared to the control groups in both sexes. Hepatocyte hypertrophy increased in both severity and incidence in all tested groups in both sexes compared to the control groups.

In the main study group, mixed microvesicular and macrovesicular fatty changes increased in the low and medium test item-treated groups in severity in the male rats. These changes increased in the medium and high doses of the test item-treated groups in severity and incidence in the females, compared to the control group. Mixed microvesicular and macrovesicular fatty changes were observed as shown in Figures 3A to 3F. At the low magnification observation, there were clear vacuolations in the hepatocyte cytoplasm, showing various severity levels. Hepatocyte hypertrophy increased in severity

and/or incidence in both sexes of all test groups, compared to the control group. Hepatocyte hypertrophy was presented in the area around the central vein, so-called the centrilobular area (zone 3), as shown in Figures 2A to 2F. At the low magnified examination, it was found that the hepatocytes surrounding the central vein (CV) were lighter in the cytoplasm and had a lower density of nuclei compared to the portal tract (PT) (zone 1). Hepatocytes in the hepatocyte hypertrophy appeared to increase in size of cytoplasm and distance between nuclei at zone 3, compared to those at zone 1. All gross findings in both sexes were microscopically confirmed as corresponding histopathological findings. In addition, minor findings were observed in the other organs and/or tissues in both sexes. However, these changes were considered as background or spontaneous lesions frequently occurred in Jcl:SD rats, which were related to various conditions such as age, sex, housing, food, and environment.

In the satellite group, mixed microvesicular and macrovesicular fatty changes were observed in the control and test groups of male rats, with similar severity and incidence. The changes were higher in severity in the test females, compared to the control females. Hepatocyte hypertrophy was observed with increased severity and incidence in the test item-treated groups in both sexes, compared to the control groups.

Histopathological changes of other tissues and organs were not related to the administration of standardized aqueous kratom leaf extract.

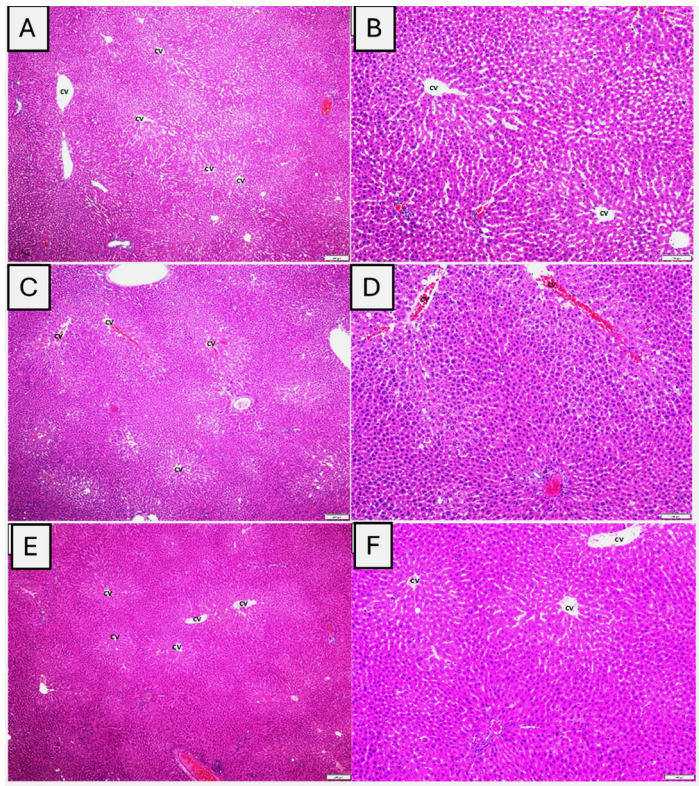

Figure 2: H&E: Hypertrophy hepatocyte in the centrilobular area (zone 3). An Increase in the size of liver cells surrounding the blood vessels of central vein. (CV): A (4X) and B (10X). Score 1; C (4X) and D (10X). Score 2 and E (4X) and F (10X) Score 4.

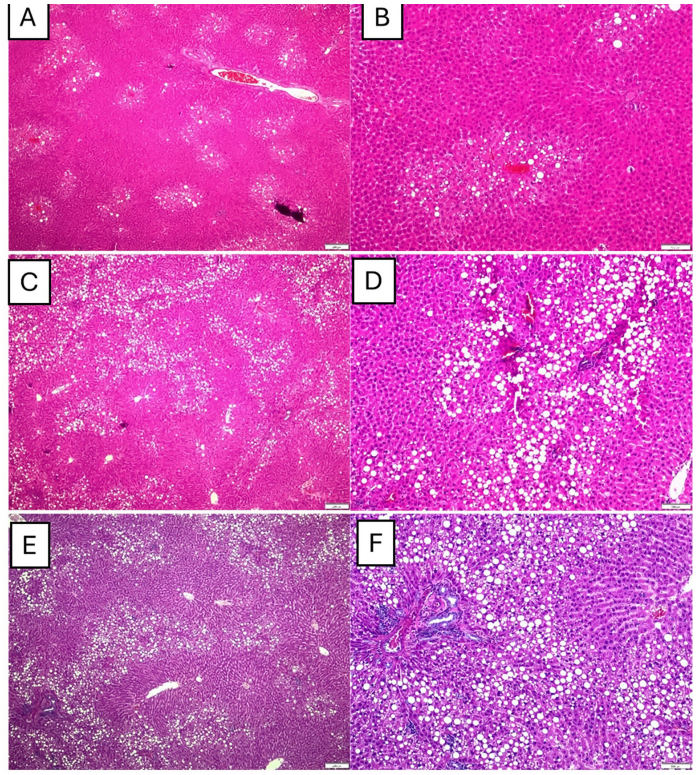

Figure 3, H&E: Fatty change with mixed micro and macrovesicular, which is an accumulation of fat in the liver cells: A (4X) and B (10X). Score 1; C (4X) and D (10X). Score 2 and E (4X) and F (10X). Score 3

Summary and Discussion of Results

This study was performed to evaluate acute and chronic toxicity effects of the test item, the standardized kratom leaf aqueous extract according to OECD Test Guideline No. 423: Acute Oral Toxicity and No. 452: Chronic Toxicity Study, respectively, to determine the maximum dose of MG in kratom that humans could consume per day.

Based on an acute toxicity study, the results showed no abnormalities during the first 30 minutes and throughout the 14-day test period after the rats were orally administered one time with kratom Leaf aqueous extract at the dose of 2000 mg/kg. The mean body weight of each rat correlated with their growth rates, and no abnormal internal organs were observed during necropsy.

From the chronic toxicity study, no abnormal clinical sign was observed in all test male and female rats after being orally administered 3 doses of the standardized kratom leaf aqueous extract, equivalent to an ADI of MG at 0.2, 1.0, and 3.0 mg/kg, for 90 and 180 days. All rats were given unlimited food and water. Some groups of rats were found to consume less food and water than usual for a few weeks. However, the average body weight gain for all rats was consistent with their growth, except for female rats receiving a high dose of extract for 90 days, who exhibited a lower body weight gain than the control group ($P<0.05$). Whereas the average body weight gain

for other groups was consistent with their growth, indicating no test-item-related influence on the rat's body weight gain.

Hematological analysis of both male and female rats that received standardized kratom leaf aqueous extract for 90 and 180 days showed some changes when compared to the control group. A reduction of red blood cell distribution width (RDW) was observed, but this was considered a non-adverse effect. Most parameters showed higher or lower values than the control values, but they were within the reference ranges. Therefore, these changes were considered as non-adverse effects. Moreover, these values in the satellite groups showed no significant differences when compared to the controls.

For clinical biochemistry test analysis, significant increases in BUN were observed in all rats that received the test item, suggesting kratom extract-related changes. Changes in ALP, ALT, globulin (GLOB), TBIL, glucose (GLU), and chloride (Cl-) were observed but were considered as non-adverse effects since these levels were within the reference ranges. Whereas the value of BUN, which was changed in the males that received a high dose of standardized kratom leaf aqueous extract for 90 days, might relate to the correlation of the increasing BUN and CRE. However, no histopathological changes of the kidney, urogenital tract, and adrenal gland were observed. Therefore, it can be concluded that this change may be related to hypovolemia conditions (Giknis, MLA, and Clifford, CB, 1999). However, no changes in hematological and blood chemistry parameters related to the test item orally administered were found within the same sex compared to the control group. Moreover, hematological and blood chemistry parameters were in the normal range (non-test item related) (Hall AP., 2012). In the satellite group, no changes in hematological and blood chemistry parameters were observed that could be related to oral administration of the test item compared to the control group. The significant increase of the ALB/GLP ratio in female rats received a high dose of the test item ($P<0.05$) compared to the control group, considering that it is not related to the orally administered standardized kratom leaf aqueous extract (non-test item related), as the non-adverse effect was found.

For pathological results, hepatocyte hypertrophy in the centrilobular area or zone 3 was observed in both male and female rats in the test item-treated group, and the severity of the changes was related to the concentration of the test item (dose-related). However, it is not related to an increase in the liver weight, while the decrease in hepatic enzyme levels, including ALT and ALP, may be related to the increase in cytochrome P enzyme activity (enzyme induction) (Hall AP., 2012). The accumulation of fat in hepatocytes (fatty change, mixed micro and macrovesicular) significantly increased, especially in female rats, suggesting a gender-related effect. The increasing of the size of hepatocytes is an adaptive cellular response, which is a reversible change. Furthermore, there were not any other changes that could be reported as harmful events. Moreover, the enlargement of the thyroid gland was observed in gross examination, which might correlate to the increase of cytochrome P activity, which induced secondary thyroid hypertrophy/hyperplasia due to stimulation of the pituitary-thyroid-endocrine axis. The histopathological examination of the ovaries found a decrease in the number of corpus luteum in both control and test groups. The test group tended to have more severity than the control

group. Due to a lack of other evidence that could support this finding, additional studies should be conducted to examine the reproductive toxicity to confirm the effect of the standardized kratom leaf aqueous extract on the reproductive system.

Based on chronic oral toxicity, the results of gross examination revealed abnormality of submandibular lymph nodes and thymus glands in some rats. However, the clinical characteristics of the lymph nodes and the thymus glands were fresh hemorrhage, which could occur during the euthanasia (perimortem) and/or during the postmortem (McInnes EF, 2012). In addition, histopathological examination of the interim kill group revealed an increase in mixed microvesicular and macrovesicular fatty changes observed in all the test item-treated groups in the females, compared to the control groups in both sexes. It was considered test item-related because the change tended to show a dose-response relationship. The change was considered non-adverse because its severity was minimal and because enzymes related to liver damage were not statistically -significant. An increase in hepatocyte hypertrophy in severity and incidence in the test item-treated groups in both sexes, compared to the control group, was considered test item-related because it tended to show a dose-response relationship. However, it was considered non-adverse because its severity was no more than slight in the males and moderate in the females, which did not cause any damage to the tissues and did not seem to be high enough to cause any functional disturbance.

In the main study, an increase in mixed microvesicular and macrovesicular fatty changes in severity was observed in the low and medium test item-treated groups in the males, and an increase in severity and incidence was observed in the medium dose and high dose test item-treated groups in the females, compared to the control groups. They were considered test item-related because the changes tended to show a dose-response relationship in severity and/or incidence. Fatty changes observed in the test item-treated males were considered non-adverse because the most severe change (severe; +4) in the test item-treated groups was just one level higher than the control group (moderate; +3). In other words, if fatty change observed in the test item-treated males had been evaluated on the basis of the level of fatty change in the control group, the changes in the low and medium doses of the test item-treated groups would have been minimal or slight in severity. Fatty change observed in the test item-treated females was considered non-adverse because the changes did not show any damage to the tissues and because the severity of fatty changes was not likely to be high enough to cause functional abnormalities of the liver.

The increases in hepatocyte hypertrophy observed in all the test item-treated groups in both sexes, compared to the control groups, were considered test item-related. This was due to the changes tending to show a dose-response relationship in severity and/or incidence. The changes were considered an adaptive response and non-adverse because most the animals showed a severity level of no more than moderate (+3), except one female in the high-dose group, and because the changes tended to decrease in severity in the female satellite group. Following a 28-day recovery period, no significant changes were observed in hematologic or clinical biochemical parameters, and the severity of hepatocellular hypertrophy in the satellite groups showed a marked reduction compared to the

main study group. Mixed microvesicular and macrovesicular fatty changes observed in the test item-treated group in male rats were considered to recover almost completely because the changes appeared similar in severity and incidence compared to the control group. However, mixed microvesicular and macrovesicular fatty changes observed in female rats of the test item-treated group were not considered to recover completely because the change was observed at a higher incidence in the test item-treated groups compared to the control group. Therefore, these changes were considered that more time is needed to recover completely in female rats of the test item-treated groups.

Conclusion

This study was performed under the principles of GLP and in accordance with OECD test guidelines to obtain information on acute and chronic toxicity effects of the test item, the standardized kratom leaf aqueous extract, after oral administration to Jcl:SD rats. The study included a single high-dose administration (acute) and repeated administration of three doses over 90 days (subchronic) and 180 days (chronic).

Based on the test results, it can be concluded that the standardized kratom leaf aqueous extract, at doses equivalent to the ADI of mitragynine in humans (0.2, 1.0, and 3.0 mg/day), is safe and does not cause oral toxicity in rats when administered repeatedly daily for periods of 90 and 180 days. This indicates that the ADI for mitragynine in humans is 3.0 mg/day, representing the maximum amount that can be consumed daily without affecting the physical health of normal people. These findings are consistent with the research study by Sabetghadam A. and colleagues, who reported test results that mitragynine in doses of 1-10 mg/kg body weight did not cause toxicity in rats, as no significant changes in blood chemistry or histological changes were observed following mitragynine administration (Sabetghadam A. et al., 2013).

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