BirEx JOURNAL
Budapest International Research in Exact Sciences
Medical, Biological, Argiculture, Engineering
Science and other related areas
e-ISSN : 2655-7827
p-ISSN : 2655-7835
http://www.bircu-journal.com/index.php/birex

Resilience State Security and the Role Sedative Agents in Military Pharmacy for State Defense in Future War

Gilang Bhakti Nusantara[1], Syahrul Tuba[2]
[1,2]*Faculty of Military Pharmacy, Universitas Pertahanan Indonesia*
syahrul.tuba@idu.ac.id

Abstract: *National defense is closely related to the role of an intelligence officer who is strong and capable of safeguarding the country's sovereignty. Intelligence covers many fields. One of those is medical intelligence. Mitragynine can be used as a sedative agent in a medical intelligence operation. To analyze a sedative agent in intelligent medical purposing of military aspect. This paper determines the role of Military Pharmacy in medical intelligence to support national defense using natural substances that contain a sedative agent. This research used narrative review method for this study obtained from Crossref, google scholar, PubMed, and Scopus range 2010 to 2021 in the English language, using the following terms: "National defense," "Medical intelligence," "Kratom" Mitragynine "Sedative agent" but we did not exclude out older works that were often cited and significant. Mitragynine binds to three types of receptors with varying affinities, with the highest affinity for μ, K, and δ-opioid receptors, which can be used as sedatives in medical intelligence to support national defense. Kratom is a plant endemic to Southeast Asia; this plant has a sedative effect at high doses. Kratom leaves contain thirty-seven alkaloid compounds. Both alkaloid compounds are Mitragynine and 7-hydroxymitragynine, both of which are included in the indole alkaloid compound, the main kratom compound. Plants that are used when facing the battlefield in maintaining national defense are very complex owned by the Indonesian state, that is the kratom plant which has a chance to strengthening people defense and security state facing of sixth generation war. This study needs to validate with more rigorous human clinical studies in the future.*
Keywords: *National defense; medical intelligence; Kratom; Mitragynine; Sedative agent*

I. Introduction

The strategic context and growth environment will bring forth the threat's nature and increasingly tricky challenges rate whether or if danger is based on the ability to comprehend, identify, and evaluate. Depending on the nature of threat, a military and non-military threats, when the source is seen as a threat from both abroad and at home, and when to do by his actors (Aritonang et al., 2018). Therefore, efforts are needed to state defense. State defense is one of the responsibilities and roles of government, which is carried out in a comprehensive, directed, integrated, and sustainable manner to meet rather complicated issues by leveraging national resources and facilities controlled by a country (www.djpp.depkumham.go.id; accessed on 5 February 2022).

Indonesia, one step forward to maintain and discuss counter-terrorism cooperation including Trafficking in Person and war using CBRNE (Chemical, Biological, Radiological, Nuclear, and Explosive) in the ASEAN forum (Wilujeng, 2021). The state constitution in Law no. 3 of 2002 concerning state defense stipulates that all efforts to defend the country's sovereignty, territorial integrity, and the safety of the entire nation from threats and disturbances to the nation's and state's integrity are the responsibility of the main component, which consist of the Indonesian National Army (TNI), a reserve component consisting of resources, which has been prepared through mobilization to strengthen the main and supporting components consisting of national resources that can be used to support the strength of the main components and the reserve components (Anwar, 2014). As a result, the

Ministry of Defense formulates policies on national defense implementation as a guideline for the Ministry of Defense and the Indonesian National Army (TNI) to achieve national defense with defense capabilities (Peraturan Menteri Pertahanan nomor 19 tahun 2015). The role of the Indonesian Army and the Ministry of Defense is crucial in handling various sectors, including medical intelligence together with the Ministry of Health (Octavian, 2021). The MOH role is to provide technical input and expertise in training, supervision and monitoring of the programme (Kuay, 2021).

Intelligence is a science that plays a vital role in supporting national defense by trying to predict, which is implemented using analysis and synthesis of information flows and by providing information involving sleep agents (Optimalisasi Kinerja Kontra Intelijen Dalam Pengamanan Rahasia Negara. Vol. 15). Another challenge that threatens national defense is the Chemical, Biological, Radiological, Nuclear, and Explosive (CBRNE) threat. Threats are every effort and activity, both from inside and outside the country against "Pancasila" and threatens or endanger the country's sovereignty, the Republic of Indonesia's territorial integrity, and the entire nation's safety stake. The threats that exist are numerous and complex, but only a few will be presented, consisting of military threats, non- military threats, and hybrid threats; however, a threat is taken in terms of CBRNE, which is a hybrid threat. In facing these threats, intelligence anticipates preparing, analyzing, and responding to potential threats that will occur. Besides that, it can also be done by identifying seven important principles consisting of CBRNE disciplines to integrate effective preparedness planning, public health disciplines, and response and medical recovery (Coleman et al., 2019).

The role of military pharmacy in the world of intelligence is included in the role of medical intelligence by implementing the disciplines that have been studied. Following the regulation of the Minister of Defense of the Republic of Indonesia number 38 of 2013, it explains that the role of medical intelligence is all efforts, jobs, and activities to carry out intelligence functions in the health sector. Health is a very important element of the quality of life in national development (Najikhah, 2021). While indirect factors such as economic factors, culture, education and work, health service facilities (Lubis, 2021). The role of a military pharmacist in the world of intelligence is by continuously observing the possibility of disease outbreaks, observing the possible spread of nuclear, biological, chemical, radiation, and explosive materials, conducting epidemiological surveillance, and carrying out epidemiological surveillance. In addition, the role in intelligence operations is important, particularly in collecting geo-medical map data to find out the strengths and weaknesses of the enemy, threats that may occur, especially related to weapons of mass destruction, or acts of terror and crime related to the use of biological, chemical, radiation, nuclear and explosive materials as well as making preparing drugs in a form of tablet which is sedative in nature (Kementerian Pertahanan Republik Indonesia. 1992; 1–3.)

One of the plant ingredients known in the pharmaceutical world that has sedative benefits is the Kratom plant (Mitragyna speciosa). This plant grows a lot in Asia, especially Southeast Asia as an endemic plant. Kratom leaves contain thirty-seven alkaloid compounds. One of these alkaloid compounds is Mitragynine and 7-hydroxy Mitragynine, both of which are included in the indole alkaloid compound, the main kratom compound. Mitragynine, which produces a significant opioid effect to produce an analgesic effect is more robust than morphine and in high doses has a sedative effect (Meireles et al., 2019). Another constituent is 7-hydroxymitragynine which exhibits a strong opioid effect (Kanato & Leyatikul, 2017). Mitragynine binds to three types of receptors with different affinities, with the highest affinity for μ, K, and δ-opioid receptors (Singh et al., 2019). This plant causes a sedative effect at high doses (Meireles et al., 2019).

II. Research Methods

The strategy of the research in this study was a narrative review. We have chosen the close relevant literature to the matter and attempted to gather information on all aspects of the role of military pharmacy in medical intelligence for state defense with sedative agents. These aspects include a sedative agent for medical intelligence to support national defense. The search was conducted using five keywords "National Defense," "Medical Intelligence," "Kratom", "Mitragynine" and "Sedative Agent" in Crossref, Google Scholar, PubMed, and Scopus range 2010 to 2021 in the English language, but we did not exclude out older works that were often cited and significant.

III. Discussion

3.1 Characteristics Mitragyna speciosa

The kratom plant, or by another name Mitragyna speciosa is one of the endemic plants from Southeast Asia. In Indonesia alone, this plant is an endemic plant of Kalimantan, which is included in the Rubiaceae tribe with straight- trunked plant morphology with brownish-gray skin. This plant can cause strong analgesic effects, sedative effects, stimulants, and antidepressant effects. From the results of empirical studies that have been carried out, these effects can appear depending on the dose given. To get a sedative effect, use very high doses of more than 15grams (Singh et al., 2019). The sedative effect is beneficial as a sedative to target the nervous system. The compounds contained in the kratom plant are 37 alkaloid compounds, the main compounds in this kratom plant are mitragynine and 7-hydroxymitragynine (Meireles et al., 2019), and it has been studied that the compound higher potent than morphine (Babu et al., 2008). Mitragynine compounds produce a significant opioid effect to produce a more potent analgesic effect than morphine. In high doses, a sedative or sedative effect is bound to three receptors with different affinities that are thirteen times more effective than morphine.

In contrast, for 7-hydroxy mitragynine, it produces the same opioid effect as morphine with (2.5, 5, 10, 20 g/infusion) kratom equivalent to (50 and 100 g/infusion) morphine through opioid. Kratom leaves contain the alkaloids mitragynine and 7 The -hydroxymitragynin which has affinity as an agonist at opioid receptors is linked to dopaminergic and GABA-ergic interneurons. Kratom activity as an agonist of μ, K and δ-opioid receptors is very potential to be developed into an analgesic with strong antinociceptive effects with weaker side effects (Ismail et al., 2019). Mitragynine has a high affinity for δ-opioid receptors mediate analgesia, respiratory depression, and euphoria. Mitraginin's antinociceptive activity is largely mediated by μ- and δ-opioid receptor subtypes. These mechanisms underlie the use of kratom as an opium substitute or reduce opium addiction and reduce pain from withdrawal symptoms. Its affinity for receptors is much lower (Meireles et al., 2019).

The chemical content of alkaloids in the kratom plant can be obtained by extraction methods using alcohol group filters such as methanol, ethanol, isopropanol, and n-butanol or through an alcohol-water mixture with maceration, sonication or Soxhlet techniques. Furthermore, the crude extract was carried out by acid-base extraction to obtain the yield of the

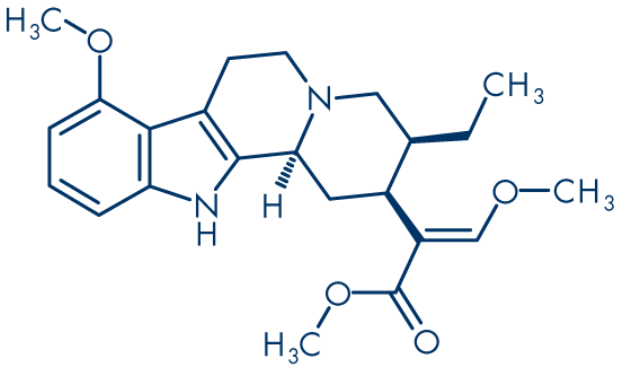

Figure 1. *Molecular Structure: Mitragynine*
(https://www.emcdda.europa.eu/publications/drug-profiles/kratom_en; Accessed 5 September 2021)

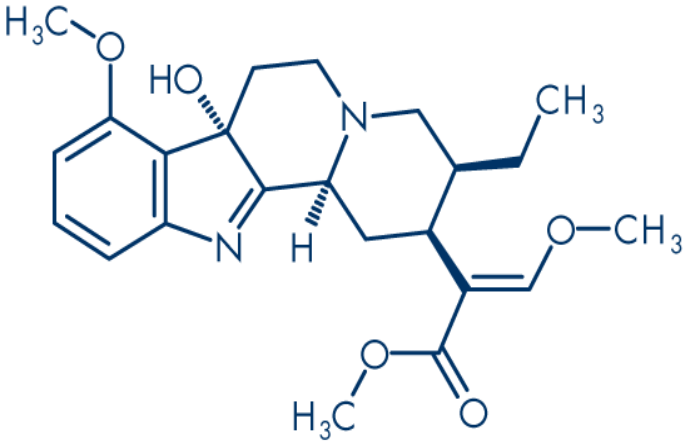

Figure 2. *Molecular Structure: 7-hydroxymitragynine*

Experts have several opinions, one of which comes from the indole alkaloid pathway with tryptamine and the monoterpene glucoside sekologanin as the main constituents. Both compounds will condense involving the enzyme strictosidine synthase (STR1) to produce strictosidine Mitragynine has a molecular weight of 398.50 g/mol is water-insoluble but soluble in traditional organic solvents such as acetone, acetic acid, alcohols, chloroform, and diethyl ether, resulting in fluorescent solutions. Mitragynine distils at 5 mmHg at 230–240 °C. It melts at 102–106 °C and creates white amorphous crystals. Mitragynine hydrochloric acid salt melts at 243°C, picrate melts at 223–224°C, and acetate melts at 223–224°C (https://www.emcdda.europa.eu/publications/drug-profiles/kratom_en; Accessed 5 September 2021).

3.2 Mechanism Sedative Effect

The Mitragynine compound blocks the Ca2+ canal. It causes inhibition of neurotransmitters, making the cessation of nerve function from it, making a person paralyzed. Moreover, it can be said that the sedative effect of kratom arises from the Mitragynine compound blocking neuronal Ca2+ which has a function as an inhibitor of the release of neurotransmitters from nerve endings in the vas deferens, besides that mitragynine also inhibits the formation of cAMP (Suhaimi et al., 2016). The two alkaloids responsible for most kratom's actions, mitragynine, and 7-hydroxymitragynine, are complete agonists of the -subtype opioid receptor (MOR). The opioid receptor antagonist naloxone counteracts the receptor agonist activity of kratom alkaloids. There are pivotal keys on the pharmacological

actions of the mitragynine such as 5-HT2a and postsynaptic α2-adrenergic receptors, and neuronal Ca2+ channels (https://www.emcdda.europa.eu/publications/drug-profiles/kratom_en; Accessed 5 September 2021).

3.3 Sedative Agent in Medical Intelligence

The content of compounds in the kratom plant has benefits that are used to immobilize enemies but are not deadly. The purpose of paralyzing the enemy is to extract information from the opponent in geo-medical conditions, troop strength, strategies, and important buildings used. The mechanism of the kratom plant as a sedative agent from the content of Mitragynine and 7- hydroxy Mitragynine is to mediate respiratory depression, analgesics, and euphoria to reduce awareness and sensitivity to external stimuli so that the enemy is not aware when being interrogated for information. This is the role of medical intelligence by preparing facilities and infrastructure to deal with a natural, non-natural, and social threat and face a possible war to prepare sedatives to immobilize the opponent and not let it die.

In general, a pharmacy that operates in the intelligence environment is included in military pharmacy. Military Pharmacy itself has a scope of work in the military and specializes in carrying out military-related activities, such as the production of drugs for war (malaria drugs), producing antibiotics, and producing symptomatic drugs for evacuation. In his practice also, a military pharmacist carries out the production of ready-to- eat food (MRE) that is sufficiently nutritious and safe, and of quality and can check drugs, food, rations that are safe and sufficient nutrition for soldiers while carrying out missions both military war operations and military operations besides war. After all that, military pharmacy is also engaged in military nutrition, cosmetics, namely the manufacture of camouflage paste used by troops to support disguise to support the success of war military operations missions, anti-insecticide lotions for combat troops in the forest, anti-shark lotions for Navy divers and moving in creating weapons of mass destruction to tackle the threat of Chemical, Biological, Radiological, Nuclear and Explosive (CBRNE) for example is the manufacture of mustard agents, neurotoxins, anthrax. So that the role of the pharmacy is to prepare decontamination materials, seizure relievers (Atropa belladonna) (Akbar, 2020), antibiotics, while in the field of radiation, it is with EDTA for chelating agents (Hashem et al., 2018).

Sishankamrata (Total People's Defense and Security System) takes crucial hand enhancing of readiness of national security in the future war to the nation (Ryacudu, 2021). The role of military pharmacy in the field of medical intelligence responds to the challenges of national defense in the CBRNE sector; among them biology weapon in terrorism is a distinct possibility one of them infectious agents and poisons are examples of biological weapons (Anderson, 2012), for example in handling covid-19 by making vaccines as well as in the manufacture of poison antidotes which are often used for sabotage in addition to challenges in the CBRNE field, preparing drugs with the independence of medicinal ingredients that empower Indonesian natural ingredients. For the manufacture of medicinal ingredients as a function of military pharmaceuticals in the field of research and science, such as the empowerment of kratom plants as sedative medicinal substances as well as the manufacture of combat nutrition and MRE for military war operations and military operations other than the war which are sufficiently safe and quality nutrition for soldiers. In its implementation, supported by the disciplines of pharmacology and toxicology, pharmacists who are engaged in medical intelligence play a role in anticipating matters related to biological weapons, chemical poisons, and the threat of radiation and explosive hazards. The aim is to find out the role of Military Pharmacy in medical intelligence to support national defense using natural ingredients that contain sedative effects as a sedative agent.

IV. Conclusion

It is the role of medical intelligence to support national defense by preparing facilities and infrastructure to face a non-natural and social natural threat and face a possible war, one of which is pharmacology and toxicology, which is to prepare sedative preparations with kratom plants. This plant can cause strong analgesic effects, sedative effects, stimulants, and antidepressant effects. From the results of empirical studies that have been conducted, these effects can appear depending on the dose of administration. With the effect that this plant has, it aims to immobilize the enemy without killing the enemy so that the enemy is not aware when being interrogated for information in the form of geo-medical conditions, troop strength, strategies, and important buildings used.

Acknowledgments

The authors would like to special thanks to the Dasuri, Lilik Hidayati, Adellia Agatha, Faculty of Military Pharmacy members, Prof. A. Octavian, Yuli Subiakto, Syahrul Tuba, Bantari Kusuma Wardhani, Editha Renesteen for supporting us in this article.

Author's Contributions

GBN as a data analyst and leading contributor in writing articles, YL as supervisor, and ST as a supervisor and review this article.

References

Akbar, S. (2020). Handbook of 200 Medicinal Plants: A Comprehensive Review of Their Traditional Medical Uses and Scientific Justifications. Handbook of 200 Medicinal Plants.

Anderson, P. D. (2012). Bioterrorism: toxins as weapons. Journal of Pharmacy Practice, 25(2), 121–129. https://doi.org/10.1177/0897190012442351

Anwar, S. (2014). The Role of Defence Diplomacy in Coping with Challenges in the Field of Defence. Jurnal Pertahanan Agustus, 4(2), 71.

Aritonang, S., Yulieanto, H., & Rajab, D. D. A. (2018). Jurnal Pertahanan. Jurnal Pertahanan, 4(1), 61–75. http://jurnal.idu.ac.id/index.php/DefenseJournal/article/view/253/pdf4

Babu, K. M., McCurdy, C. R., & Boyer, E. W. (2008). Opioid receptors and legal highs: Salvia divinorum and Kratom. Clinical Toxicology, 46(2), 146–152. https://doi.org/10.1080/15563650701241795

Coleman, C. N., Bader, J. L., Koerner, J. F., Hrdina, C., Cliffer, K. D., Hicks, J. L., James, J. J., Mansoura, M. K., Livinski, A. A., Nystrom, S. v., DiCarlo-Cohen, A., Marinissen, M. J., Wathen, L., Appler, J. M., Buddemeier, B., Casagrande, R., Estes, D., Byrne, P., Kennedy, E. M., … Hatchett, R. (2019). HHS Public Access Author manuscript Disaster Med Public Health Prep. Author manuscript; available in PMC 2020 July 04. Published in final edited form as: Disaster Med Public Health Prep. 2019 December ; 13(5-6): 995–1010. doi:10.1017/dmp.2018.163. Chemica. Disaster Med Public Health Prep., 13(5–6), 995–1010. https://doi.org/10.1017/dmp.2018.163.Chemical

European Monitoring Centre for Drugs and Drug Addiction. Kratom drug profile. Small Ruminant Research [Internet]. 1994; 14(2):151–9. https://www.emcdda.europa.eu/publications/drug-profiles/kratom_en; Accessed 5 September 2021

Hashem, A. M., Abdel-Ghany, A. E., Abuzeid, H. M., El-Tawil, R. S., Indris, S., Ehrenberg, H., Mauger, A., & Julien, C. M. (2018). EDTA as chelating agent for sol-gel synthesis of spinel LiMn2O4 cathode material for lithium batteries. Journal of Alloys and Compounds, 737, 758–766. https://doi.org/10.1016/j.jallcom.2017.12.153

Indonesia NR, Rahmat D, Yang T, Esa M, Indonesia PR. www.djpp.depkumham.go.id. 1982;
Ismail, I., Wahab*, S., Sidi, H., Das, S., & Razali, L. J. L. and R. (2019). Kratom and Future Treatment for the Opioid Addiction and Chronic Pain: Periculo Beneficium? In Current Drug Targets (Vol. 20, Issue 2, pp. 166–172). https://doi.org/http://dx.doi.org/10.2174/1389450118666170425154120
Kanato, M., & Leyatikul, P. (2017). Effectiveness of Drug Camps in Treatment of Substance Abuse in Thailand. Journal of Community Health, 42(6), 1090–1095. https://doi.org/10.1007/s10900-017-0356-1
Kuay, L.K., et.al. (2021). Methodology of the Evaluation of "Komuniti Sihat Pembina Negara-Plus" (KOSPEN Plus) Programme among Workers in Malaysia (Phase 1). Budapest International Research in Exact Sciences (BirEx) Journal Vol 3 (1):68-76.
Lubis, D.A., et.al. (2021). The Relation between the Characteristics of Parents and the Incidence of Stunting in Elementary School Children in the Working Area of the Air Beliti Health Center. Budapest International Research in Exact Sciences (BirEx) Journal Vol 3 (4): 254-260.
Meireles, V., Rosado, T., Barroso, M., Soares, S., Gonçalves, J., Luís, Â., Caramelo, D., Simão, A., Fernández, N., Duarte, A., & Gallardo, E. (2019). Mitragyna speciosa: Clinical, Toxicological Aspects and Analysis in Biological and Non-Biological Samples. Medicines, 6(1), 35. https://doi.org/10.3390/medicines6010035
Menteri Pertahanan. Peraturan Menteri Pertahanan nomor 19 tahun 2015 tentang kebijakan penyelenggaraan pertahanan negara tahun 2015-2O19. 2016; 2:35.
Najikhah, N., et.al. (2021). Determinants of Complete Basic Immunization in Children Aged 12-23 Months in Indonesia. Budapest International Research in Exact Sciences (BirEx) Journal Vol 3 (4): 304-318.
Octavian, A. (2021). National defense perspective of the COVID-19 pandemic. IOP Conference Series: Earth and Environmental Science, 708(1). https://doi.org/10.1088/1755-1315/708/1/012103
Optimalisasi Kinerja Kon Tra Intelijen Dalam Peng Amanan Rahasia Negara. Vol. 15, Optimalisasi Kinerja KonTra Intelijen Dalam Peng Amanan Rahasia Negara. 2016. p. 17–29.
Ryacudu. (2021). Strengthening Total People's Defense and Security System in the Industrial Revolution Era 4. 0 To Face. 7(2), 191–204.
Singh, D., Narayanan, S., Grundmann, O., Dzulkapli, E. bin, & Vicknasingam, B. (2019). Effects of Kratom (Mitragyna Speciosa Korth.) Use in Regular Users. Substance Use & Misuse, 54(14), 2284–2289. https://doi.org/10.1080/10826084.2019.1645178
Suhaimi, F. W., Yusoff, N. H. M., Hassan, R., Mansor, S. M., Navaratnam, V., Müller, C. P., & Hassan, Z. (2016). Neurobiology of Kratom and its main alkaloid mitragynine. Brain Research Bulletin, 126, 29–40. https://doi.org/https://doi.org/10.1016/j.brainresbull.2016.03.015
Wilujeng, N. F. (2021). Jurnal Pertahanan Regional Forum (ARF) From the Perspective of. 7(2), 205–216.