The Potential of Red Betel Leaf Essential Oil (Piper Crocatum Ruiz & Pav) as an Anti-Bleeding in the Management of Corona Virus Infection

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Abstract
Coronavirus can also harm the vascular system and cause bleeding; this damage to the vascular system might be followed by dysfunctions in other body systems, therefore not a few COVID-19 survivors have experienced a stroke as a complication of COVID-19. Bleeding that occurs in the nose is a common condition that occurs as a result of a person's injury, allergies, or platelet levels that are declining. There are several simple ways to stop this bleeding, but for Indonesians betel leaf is a widely chosen traditional treatment. The subjects of experimental animal studies were divided into 4 groups. The results of the Anova test analysis showed that there was a significant difference in average platelet levels (p=0.05) in the 4 groups. The results showed that the lowest average thrombocytes and hematocrit levels were found in group 2, namely the group that was given LPS without being given betel leaf essential oil. The highest average thrombocytes and hematocrit levels were found in group 3, namely the group that was first given betel leaf essential oil, after which it was only applied LPS. Red Betel Leaf Essential Oil has the potential as an anti-bleeding in research subjects induced with infectious materials characterized by increasing average platelet levels and Hematocrit as components that play a role in the blood clotting process.

Keywords: betel leaf essential oil, thrombocytes, anti bleeding

Introduction

At the beginning of the year 2020, the world was rocked by the rapid spread of a new strain of pneumonia that was given the name coronavirus disease 2019 (COVID-19). This strain of pneumonia was caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). This pandemic has had a far-reaching impact on the economy, social interactions and lifestyles of individuals especially on human health such as disorders of the respiratory system. (Huang et al., 2020).

Infection with the Corona virus has traditionally been thought of as a disease

of the respiratory system; however, recent advances in medicine have revealed that there is involvement across multiple systems, including neurological manifestations. There is abundant evidence to suggest that the effects of COVID-19 are not necessarily restricted to the respiratory system, but rather can also interfere with the cardiovascular system, the gastrointestinal system, the urinary system, the reproductive system, and the brain system (Li et al., 2020). Neurological signs that might occur in individuals who have an infection with the Coronavirus.

Corona virus can decrease immune function via an inflammatory response, and greater viral replication results from the activation of the kappa B nuclear factor transcription pathway (NF-B) known as cytokine storm (Camini et al., 2017). In this cytokine storm reaction, a large number of anti-inflammatory agents, including interleukin-1, interleukin-6, and tumour necrosis factors, are released, and immune cells are overactivated. Systemic inflammatory response syndrome is caused by cytokine storms. SIRS can result in systemic endothelial (vascular wall) damage and hypercoagulation, which increases the risk of macrothrombosis and microthrombosis. Coronavirus can also harm the vascular system and cause bleeding; this damage to the vascular system might be followed by dysfunctions in other body systems, therefore not a few COVID-19 survivors have experienced a stroke as a complication of COVID-19 (Safithri, 2012).

The biodiversity of Indonesia holds significant promise for the development of novel antioxidant chemicals. Antioxidant-containing plant parts include roots, stems, bark, twigs, leaves, fruits, flowers, and seeds. The red betel plant (Piper crocatum), which is widely used as an attractive plant and a medicinal herb, has not been utilised to its full potential in recent years (Kumari and Nirmala, 2015). Bleeding that occurs in the nose is a common condition that occurs as a result of a person's injury, allergies, or platelet levels that are declining. There are several simple ways to stop this bleeding, but for Indonesians betel leaf is a widely chosen traditional treatment. Red betel leaf metabolite compounds are reported to contain essential oils, flavonoids, alkaloids, tannins, saponins and polyphenols (Insanu et al, 2017).

The bioactive compound of red betel leaf has the potential to be anti-diabetic (Bharti et al., 2018; Weni et al, 2020), anti-inflammatory (Maslikah et al., 2016), immunomodulators (Hartini et al., 2014), antioxidants (Boutennoun et al., 2017; Fatmawaty et al., 2019), anti-microbial and cytotoxic (Astuti et al. 2014; Parfati et al, 2016).

This research is expected to contribute that the content of tannins and flavonoids in red betel leaves can be used as phytopharmaceutical ingredients against the management of corona virus infection through anti-inflammatory and anti-bleeding approaches so that cytokine storms and complications such as

hemorrhage in the brain or stroke do not occur.

Materials and Methods

Ethical approval

The research was conducted after obtaining Ethical Clearance from the Animal Research Ethics Committee of the Faculty of Mathematics and Natural Sciences - University of North Sumatra (Animal Research Ethics Committees / AREC) No. 0500 / KEPH-FMIPA / 2022.

Subject

The subjects of experimental animal studies were divided into 4 groups: Group P1; Rats were given red betel leaf essential oil 10 mg/Kg Body weight of rat by oral for 14 days. Furthermore, the animal is executed under anesthesia using Chlorofom to draw blood from the heart. Group P2: Rats were only induced with Lipopolosaccharide (LPS) Escheria coli, then day 4 after there were inflammatory signs execution was carried out under anesthesia using Chlorofom to draw blood from the heart. Group P3: Rats were given red betel leaf essential oil of 10 mg/Kg Body weight of rat by oral for 14 days. On the 10th day induced with Lipopolosaccharide (LPS) Escheria coli, the 14th day after there were inflammatory signs execution was carried out. Group P4: Rats induced with Lipopolosaccharide (LPS) Escheria coli, day 4 in betel leaf extract 10 mg/Kg Body weight of rat by oral for 10 days then the animals tried to be executed under anesthesia using Chlorofom to draw blood from the heart. Thrombocytes level examination is carried out using a hematology analyzer. Statistical analysis using the Anova Test.

Results and Discussion

The average platelet levels (p=0.05) in the 4 groups. The results showed that the lowest average thrombocytes and hematocrit levels were found in group 2, namely the group that was given LPS without being given betel leaf essential oil. The highest average thrombocytes and hematocrit levels were found in group 3, namely the group that was first given betel leaf essential oil, after which it was only applied LPS (Table 1).

Table 1. The average number of thrombocytes and hematocrit

Variable	P1 Group	P2 Group	P3 Group	P4 Group	Anova
	Mean ± Sd	Mean ± Sd	Mean ± Sd	Mean ± Sd	P
Thrombocytes	976 ± 120.96	846.67 ± 188.53	1129.50 ± 260.13	895.83 ± 137.65	0.05
Hematocrit	44.62 ± 3.82	40.42 ± 5.06	44.80 ± 7.06	41.53 ± 3.82	0.366

Note: * = significant (p<0,05); sd: standard deviation

According to the findings of the research conducted, the rats in group 3 were protected initially by the administration of red betel leaf essential oil, and then they were made sick by the administration of Lipopolosaccharide (LPS) Escheria coli. The results showed the highest average platelets and hematocrit compared to other groups. Flavonoids contained in the essential oil of red betel leaves have the ability to work as antioxidants by donating hydrogen ions so that molecules become more stable and non-radical, capturing and warding off free radicals (scavengers) so that platelet levels increase.

It has been found that the amount of phenolic chemicals (flavonoids) that can act as antioxidants in red betel leaves is significantly higher than in green betel leaves. Because of their high flavonoid content, red betel leaves have the potential to operate as antioxidants, and an extract of red betel leaves made with methanol has been found to have antiproliferative effects.Antioxidants are needed to neutralize free radicals in preventing oxidative stress and have an anti-inflammatory effect so that they can be used to strengthen the immune system and protect the body from the risk of being infected with the corona virus.

The main compounds that play a role in the blood clotting process are tannins and flavonoids (Rahayu et al., 2011). The pharmacological effects of tannins are as astringent, healing, antiseptic, antioxidant, vasoconstrictor, hemostatic, anti-pathogenic microbial, anti-cancer and anti-diabetic (Bele et al., 2010).

The mechanism of action of tannins as vasoconstrictors is through their astringent effect (Klatoe et al., 2012). Another compound contained in the betel plant that functions as an anti-bleeding is flavonoids. The mechanism of flavonoids in the cessation of bleeding is by vasoconstriction mechanism (Dougnon et al, 2012).

The content of tannins and flavonoids in betel leaves can affect bleeding time. Flavonoids and tannins contained in betel leaves are thought to play a role in inhibition of local synthesis and production of prostaglandin I2 vasodilation (prostacyclines) thus causing the process of wound contraction (vasoconstriction) to be faster (Salawu et al., 2008).

Tannins are one of the components responsible for the secretion of 5-hydroxytryptamin (serotonin) and thromboxane A2 (Sari et al., 2013). Serotonin and thromboxane A2 are compounds that are secreted due to a response to thrombocytes activation attached to the damaged walls of blood vessels.

Serotonin has a function as a powerful vasoconstrictor, while thromboxane A2 in addition to also functioning as a vasoconstrictor, plays a role in the activation process of adjacent thrombocytes and due to the sticky nature of these additional thrombocytes, it will cause it to adhere to platelets that were originally already active (platelet aggregation) (Pignatelli et al., 2006).

This thrombocytes activation cycle continues, causing the withdrawal of even more additional platelets to form thrombocytes plugs. These plugs are initially loose, but can usually successfully block blood loss when the wound in the blood vessel is small, but when the wound is large, a blood clotting mechanism is needed to stop the bleeding (Guyton, 2014).

Conclusion

Red Betel Leaf Essential Oil has the potential as an anti-bleeding in research subjects induced with infectious materials characterized by increasing average platelet levels and Hematocrit as components that play a role in the blood clotting process.

Conflict of Interest

No potential conflicts of interest

Acknowledgement

The authors of the study extend gratitude to everyone who volunteered to participate in the research. This work was financed by study contract number 0180/UN33.8/PPKM/PT/2022 from the Ministry of Education, Culture, Research, and Technology, State University of Medan.

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