



MEDICINAL PLANTS FOR TREATMENT OF IDIOPATHIC THROMBOCYTOPENIC PURPURA: A REVIEW

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ABSTRACT

When platelets are destroyed by cellular and antibody-mediated processes, this is known as idiopathic thrombocytopenic purpura (ITP), which is an autoimmune disorder. Multiple research studies have documented the potential therapeutic applications of various Indonesian plants for ITP. These plants include *Tribulus terrestris*, *Tinospora cordifolia*, *Lycenium barbarum*, *Oryza sativa*, *Carica papaya*, and *Psidium guajava*. It has been demonstrated that these plants elevate platelet counts and reduce oxidative stress in ITP patients. This article attempts to provide a synopsis of several Indonesian plants that have been utilized in vivo and in vitro to treat ITP.

KEYWORDS: Idiopathic thrombocytopenic purpura, *Tribulus terrestris*, *Tinospora cordifolia*, *Lycenium barbarum*, *Oryza sativa*, *Carica papaya*, *Psidium guajava*.

INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disease in which platelets are destroyed by cells and antibodies.^[1] Acute patients often present with clinical symptoms of bleeding and platelet counts below 30,000, indicating damage to circulating platelets and suppression of platelet production in the bone marrow.^[1] With the absence of clinically evident secondary immune thrombocytopenia, the presence of isolated thrombocytopenia below $100 \times 10^9/L$, and the exclusion of other etiological factors, the diagnosis of this condition is generally straightforward.^[2, 3] Nearly 30 new cases of the disease are identified annually, although this figure fluctuates by region. Age increases the incidence rate of this disease, which is more prevalent in women.^[4] Conversely, the success rate of curing this ailment in children exceeds 70%.^[5] On the contrary, ITP is a more intricate condition that typically manifests gradually in adults without any discernible symptoms. This persistent disease frequently develops subsequent to a viral infection or another medical condition.^[5] The objective of this review is to analyze the research outcomes concerning potential therapeutic applications of Indonesian plants for idiopathic thrombocytopenic purpura (ITP).

Tribulus terrestris

Tribulus terrestris is an annual plant indigenous to the Mediterranean region and a member of the *Zygophyllaceae* family. Long stems, small yellow flowers, and large spines adorn the fruit of *T. terrestris*.^[6] Active compounds, including alkaloids, flavonoids, and saponins, are present in this plant. An advantageous characteristic of *T. terrestris* is its capacity to alter blood parameters or increase platelet activity.^[7] According to clinical research, platelet counts in patients with ITP can be increased by 10 mg/kg/day of *T. terrestris*.^[8] Patients diagnosed with ITP typically exhibit a platelet count that is below $100 \times 10^3/\mu L$.^[9]

Tinospora cordifolia

Tinospora cordifolia is a plant belonging to the *Menispermaceae* family that has the nickname "nectar of life" because of its benefits for the immune system and the balance of various body organs.^[10] *T. cordifolia* has a stem with a mouse structure, and in the cross section there is yellow wood composed of wedge-shaped wood bundles with large veins oriented radially and separated by narrow medullary rays. It has heart-shaped leaves made of a thin, waterproof membrane. The flowers are small, unisexual, and yellow.^[11] *T. cordifolia* has many benefits that can be used to treat various medical conditions, such as fever, urinary tract problems, diarrhea, skin diseases, leprosy, diabetes, and many

more. *T. cordifolia* is reported to have antibacterial, antipyretic, immune-modulatory, analgesic, smooth muscle relaxant, antioxidant, cardio-protective, and hypoglycemic properties. On the other hand, *T. cordifolia* has alkaloids, steroids, glycosides, sesquiterpenoid, phenolics, aliphatic chemicals, and a few polysaccharides.^[12] *T. cordifolia* plant has been reported to increase platelet counts in ITP patients at a dose of 100 mg/kg.^[11]

Lycium barbarum

Lycium barbarum is a member of the *Solanaceae* family. For millennia, the red fruit of *L. barbarum* has been employed in traditional Chinese herbal medicine.^[13] One of the biological activities and pharmacological functions of this plant has been documented to be the ability to increase platelet count and decrease oxidative stress.^[14] According to in vivo investigations, platelet counts in mice with immune thrombocytopenic purpura are significantly increased by *L. barbarum* polysaccharides at doses of 50, 100, 200, and 400 mg/kg/day for seven days.^[15] The findings indicate that the platelet count tripled from the stable condition to the point where it reached 100 mg/kg/day. The significance of *L. barbarum* polysaccharides in the immune treatment of thrombocytopenic purpura is demonstrated.^[16]

Oryza sativa

Red yeast rice, or what is commonly known as *Oryza sativa*, is the result of rice fermentation by the mold *Monascus purpureus*. As a traditional medicine, *O. sativa* has many benefits, including restoring platelet counts and maintaining erythrocyte, hemoglobin, and hematocrit levels within normal limits. Lovestatin and vitamin B12 are bioactive compounds that are found in *O. sativa*. They are secondary metabolites that can raise the number of platelets.^[17] In vivo research results report that administration of *O. sativa* at a dose of 400 mg/kg/day can increase the number of erythrocytes, hematocrit, and platelets in thrombocytopenia patients.^[18]

Carica papaya

Carica papaya is a plant belonging to the *Caricaceae* family. This plant is a two-seed plant, diploid, and polygamous.^[19] Basically, this plant has properties as an anti-inflammatory, anti-tumor, antioxidant, and immunomodulatory agent.^[20] *C. papaya* leaf extract has long been used as a treatment for thrombocytopenia^[21], where this plant extract contains proteolytic enzymes such as papain and chymopapain, which can increase the number of platelets.^[21] Platelet counts goes up in people with ITP taking *C. papaya* leaf extract tablets three times a day for seven days, according to results from a clinical study.^[22]

Psidium guajava

Psidium guajava is a plant that is widely used in traditional medicine in various countries.^[23] *P. guajava* leaf extract has been shown to increase platelet counts in both humans and animals.^[24] The results of in vivo research show that administration of *P. guajava* at doses

of 150 and 300 mg/kg/day for 15 days can increase the number of rat platelets.^[25] This is because the quercetin content contained in *P. guajava* leaves can increase the expression level of SCF mRNA in bone marrow stromal cells, which can stimulate platelets by inducing the liver to secrete thrombopoietin.^[26-28]

CONCLUSION

It has been scientifically demonstrated that each of these plants can increase platelet count in idiopathic thrombocytopenic purpura; however, the specific mechanism by which each plant increases platelet count or restores platelet count to normal varies between plants. To determine whether this plant is effective as a novel alternative treatment for idiopathic thrombocytopenic purpura, additional research is required.

REFERENCES

- Gómez-Almaguer D. Adult patients with immune thrombocytopenic purpura. New expectations. *Medicina Universitaria*, 2014; 16(65): 219-221.
- Rodeghiero F, Stasi R, Gernsheimer T, Michel M, Provan D, Arnold DM, *et al.* Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood.*, 2009; 113(11): 2386-2393.
- Provan D, Stasi R, Newland AC, Blanchette VS, Bolton-Maggs P, Bussel JB, *et al.* International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood.*, 2010; 115(2): 168-186.
- Schoonen WM, Kucera G, Coalson J, Li L, Rutstein M, Mowat F, *et al.* Epidemiology of immune thrombocytopenic purpura in the general practice research database. *Br J Haematol*, 2009; 145(2): 235-244.
- George JN, el-Harake MA, Raskob GE. Chronic idiopathic thrombocytopenic purpura. *N Engl J Med.*, 1994; 331(18): 1207-1211.
- Wu G, Jiang S, Jiang F, Zhu D, Wu H, Jiang S. Steroidal glycosides from *Tribulus terrestris*. *Phytochemistry*, 1996; 42(6): 1677-1681.
- Gauthaman K, Ganesan AP, Prasad RN. Sexual effects of puncturevine (*Tribulus terrestris*) extract (protodioscin): An evaluation using a rat model. *J Altern Complement Med.*, 2003; 9(2): 257-265.
- Aghapour S, Mostafaie A, Payandeh M, Mansouri K, Sohrabi F, Koolivand Z. Effect of aqueous extract of *Tribulus terrestris* on the activity of major platelets factors and the treatment of immune thrombocytopenic purpura. *Health Med Res J.*, 2022; 1(1): 16-21.
- McCrae K. Immune thrombocytopenia: No longer 'idiopathic'. *Cleve Clin J Med.*, 2011; 78(6): 358-373.
- Sharma B, Dabur R. Protective effects of *Tinospora cordifolia* on hepatic and gastrointestinal toxicity induced by chronic and moderate

- alcoholism. *Alcohol and Alcoholism*, 2016; 51(1): 1-10.
11. Shinde, D, L., Pawar, V, B., Katkar, S, R., Kulkarni, S. Study of Guduchi kwath (*Tinospora cordifolia*) In patients of dengue fever with thrombocytopenia. *J Surv Fish Sci.*, 2023; 10(4S): 3166-3174.
 12. Upadhyay AK, Kumar K, Kumar A, Mishra HS. *Tinospora cordifolia* (Willd.) Hook. f. and Thoms. (Guduchi) - validation of the Ayurvedic pharmacology through experimental and clinical studies. *Int J Ayurveda Res.*, 2010; 1(2): 112-121.
 13. Gao Y, Wei Y, Wang Y, Gao F, Chen Z. *Lycium barbarum*: A traditional chinese herb and a promising anti-aging agent. *Aging Dis.*, 2017; 8(6): 778-791.
 14. Xiao J, Liong EC, Ching YP, Chang RC, So KF, Fung ML, *et al.* *Lycium barbarum* polysaccharides protect mice liver from carbon tetrachloride-induced oxidative stress and necroinflammation. *J Ethnopharmacol*, 2012; 139(2): 462-470.
 15. Kwok SS, Bu Y, Lo AC, Chan TC, So KF, Lai JS, *et al.* A systematic review of potential therapeutic use of *Lycium barbarum* polysaccharides in disease. *Biomed Res Int.*, 2019; 2019: 1-18.
 16. Li XM, Ma YL, Liu XJ. Effect of the *Lycium barbarum* polysaccharides on age-related oxidative stress in aged mice. *J Ethnopharmacol*, 2007; 111(3): 504-511.
 17. Syam Y, Setiadji R, Djide N, Patellongi I. Red angkak effects (*Monascus purpureus*) to the platelet enhancement of patients with dengue fever in lontara IV care unit in RSUP DR. Wahidin Sudirohusodo Makassar. *Int J ChemTech Res.*, 2017; 10(1): 378-382.
 18. Hasim, Adrianto D, Satyaningtjas A, Rosary F. Combination of angkak (red yeast rice), red guava (*Psidium guajava* Linn) leaf extract and red guava fruit juice increase thrombocyte in quinine-exposed rats. *IOSR J Pharm.*, 2015; 5(4): 1-6.
 19. Arumuganathan K, Earle ED. Nuclear DNA content of some important plant species. *Plant Mol Biol Rep.*, 1991; 9(3): 208-218.
 20. Owoyele BV, Adebukola OM, Funmilayo AA, Soladoye AO. Anti-inflammatory activities of ethanolic extract of *Carica papaya* leaves. *Inflammopharmacol*, 2008; 16(4): 168-173.
 21. Gurung S, Skalko-Basnet N. Wound healing properties of *Carica papaya* latex: In vivo evaluation in mice burn model. *J Ethnopharmacol*, 2009; 121(2): 338-341.
 22. Otsuki N, Dang NH, Kumagai E, Kondo A, Iwata S., Morimoto C. Aqueous extract of *Carica papaya* leaves exhibits anti-tumor activity and immunomodulatory effects. *J Ethnopharmacol*, 2010; 127(3): 760-767.
 23. Shruthi DS, Roshan A, Timilsina SS, Sunita S. A review on the medicinal plant *Psidium guajava* Linn. (Myrtaceae). *Drug Deliv Ther.*, 2013; 3: 162-168.
 24. Kummee P, Borisutpeth M, Chanlun S, Kanbutra P, Chanlun A. Efficacy of guava leaf extract as alternative pre-milking teat dipping in reducing teat-end bacterial load of milking dairy cows. *Int J Pharm Pharm Sci.*, 2015; 7: 434-438.
 25. Bordoloi P, Devi D, Dasgupta S. A comparative study of the platelet augmentation potential of leaf extracts of *Psidium guajava* with *Carica papaya* in thrombocytopenic rats. *Sch J App Med Sci.*, 2016; 4(8A): 2774-2782.
 26. MacNeil AJ, Junkins RD, Wu Z, Lin TJ. Stem cell factor induces AP-1-dependent mast cell IL-6 production via MAPK kinase 3 activity. *J Leukoc Biol.*, 2014; 95(6): 903-915.
 27. Kaser A, Brandacher G, Steurer W, Kaser S, Offner FA, Zoller H, *et al.* Interleukin-6 stimulates thrombopoiesis through thrombopoietin: Role in inflammatory thrombocytosis. *Blood*, 2001; 98(9): 2720-2725.
 28. Kaushansky K. The molecular mechanisms that control thrombopoiesis. *J Clin Invest*, 2005; 115(12): 3339-3347.