

Medicinal Plants Explain The Significant Role of Uric Acid for Malaria Parasite

Abstract:

Medicinal plants, recognized and employed in conventional medicine practices since prehistoric era. Plants produce thousands of chemical substances for functions counting defence against insects, fungi, bacterial and parasitic diseases.

Malaria is most widespread parasitic infection , it caused by coccidian protozoa of the genus plasmodium , four species are mostly infect human, P.falciparum, P.vivax, P. Malriae and P.ovale, Majority of malaria cases resulted from P.falciparum and P.vivax.

Uric acid regarded as one of the damaging molecular patterns of malaria parasite infection , and in this review we discussed the potential role of medicinal plants used as antimalarial to diminish the level of uric acid in gout patients. These may suggest that most of the complication associated with malaria ,may attributed to amplified level of uric acid . Experimental studies recommended.

Keywords: Uric acid, Malaria parasite, Medicinal Plants, Malaria and hyperuricemia

Background

A medicinal plant defined as any plant which, in one or more of its organs, holds essences that applied for curative goals or which are precursors for the production of useful medicines [1].

Malaria is a disease resulted from recurring cycles of growth of the parasite Plasmodium in the red blood cell [2]. Uric acid (UA) is the ending product of purine metabolism in human beings owing to the loss of uricase action by different mutations of its gene through the Miocene epoch, which led to humans having superior UA concentrations than other mammals. Also, 90% of UA filtered by the kidneys reabsorbed, not being excreted [3].

Uric acid is promising as a chief inflammatory molecule in malaria. Not merely is uric acid detected in the precipitated shape in infected red blood cells, but high levels of hypoxanthine, a precursor for uric acid, also build up in infected red blood cells. Both produced upon infected red blood cell burst into the circulation where hypoxanthine would be transformed into uric acid and precipitated uric acid would activate immune cells. Uric acid is an essential contributor to inflammatory cytokine production, dendritic cell and T cell responses provoked by *Plasmodium*, suggestive of uric acid as a new molecular target for anti-inflammatory remedies in malaria [4].

Discussion:

Cinnamon (*Cinnamomum zeylanicum*, and *Cinnamomum cassia*), the everlasting tree of tropical medicine, member to the Lauraceae family. It is one of the most significant spices used every day by people all over the globe. It mainly holds essential oils and other derivatives, such as cinnamaldehyde, cinnamic acid, and cinnamate. Also being, anti-inflammatory, antimicrobial, an antioxidant, anticancer, antidiabetic, lipid-lowering, and cardiovascular-disease-lowering compound, it has also been recorded to have actions against neurological troubles, such as Parkinson's and Alzheimer's diseases [5].

Study done by Yeti Nurhayati and Tresia Umarianti found that; Decoction cinnamon with honey can lower uric acid concentration between gout patients [6]. Study done by Attieh A. Hanadi et. al set up that, cinnamon's crude water -soluble extracts capacity to suppress β -hematin configuration (malaria pigment/ hemozoin) in vitro [7].

Study done by Parvazi S et.al, identified that cinnamon has an inhibitory impact on *Plasmodium falciparum in vitro* with IC50 of 1.25 mg/mL with importance of $p < 0.001$. The modified metabolites are succinic acid, glutathione, beta-alanine, L-aspartic acid, and 2-methylbutyryl glycine and the chief metabolic cycles influenced were alanine, aspartate, and glutamate pathway, pantothenate and coenzyme A biosynthesis, lysine biosynthesis, and glutathione metabolism, all of which are significant as antimalarial targets [8].



Figure NO 1: shows organic Cinnamon.

Turmeric, a dried powder resulting from the rhizome of *Curcuma longa*, used for centuries in particular regions of the world and connected to many biological actions counting, antimicrobial, antigrowth, antioxidant, anti-inflammatory, anti-arthritic, anticancer, anti-atherosclerotic, antidepressant, anti-aging, antidiabeticwound healing, and memory-enhancing actions [9].

Study done by Mustafa Kiyani M et al showed that; Uric acid concentrations were considerably decreased after treatment with turmeric nanoparticles (T-NPs), signifying that T-NPs show higher potential against gout control [10].

research done by Raju C et al identified that; curcumin, a poly-phenolic organic particle resulting from turmeric, suppresses chloroquine-resistant *Plasmodium falciparum* development in culture in a dose dependent method by an IC_{50} of $\sim 5 \mu M$. Also, oral administration of curcumin to mice infected with *Plasmodium berghei* lowers blood parasitemia by 80-90% and promotes their survival considerably [11].



Figure NO 2: shows fresh turmeric

Study done by Büsing F et al revealed that; In spite of its sugar content, usual use of large quantities of OJ do not boost the danger of gout but may even take part to lower uric acid concentrations [12]. study done by Adumanya O. C et al showed that; Multiple-drug remedies that contain a non-antimalarial drug like vitamin E and orange fruit juice to promote the antimalarial impact of a blood schizontocidal drug , but are not regarded as combination remedy [13].



Figure NO 3: shows orange juice

Ginger, *Zingiber officinale* Roscoe, is a spice employed as a medicinal plant in several regions. Study done by Shivraj Hariram Nile and Se Won Park showed that; Ginger rhizome portions and its active components having hopeful antiinflammatory, antioxidant, and anti-gout characters and might be employed as probable natural medicine against oxidative stress and inflammatory associated diseases after flourishing in vivo study and clinical trials [14]. Study done by Li J revealed that; Ginger-partitioned moxibustion has much effectiveness on malaria in Congo [15].



Figure NO 4: shows ginger

Study done by Hongjing Wang et al showed that; The lemon fruit juice and/or the water -soluble extracts considerably decreased serum uric acid concentrations in both human beings and mice [16]. Study done by Shija KM et al revealed that; Lemon decoction confirmed antimalarial action in mice infected with *P. berghei* ANKA through parasites inhibition by 39% as contrasted to those received placebo. but, when used alone, lemons did not enough as a treatment but combination with standard antimalarials, lemons enhanced early parasite removal with superior hematological parameters [17].



Figure NO 5: shows : Lemon juice

Study done by Ramesh and Thivyah showed that; Apple cider vinegar has a possible anti-inflammatory agent in gout management [18]. Besides apple cider vinegar considered as one of the most effectual home therapies for malaria [19].



Figure NO 6: shows Apple cider vinegar

Study done by Mehmood A et al showed that; Grapefruit juice considerably up-regulated ABCG2 protein expression in the small and large bowel, recommended that grapefruit juice employed as a urate reducing agent [20]. Study done by Olayemi, S.O showed that; the pre-treatment of mice with grapefruit juice for one week postponed the establishment P.berghei parasitemia [21].



Figure NO7: shows grapefruit juice

Conclusion:

Fortunately most of medicinal plants used for lowering uric acid concentration can also suppress the growth of malaria parasite that indicating importance of uric acid and /or its precursors , mainly hypoxanthine for erythrocytic cycle of malaria parasite. Experimental studies recommended using several anti-malarial medicinal plants.

References:

1. Sofowora A, Ogunbodede E, Onayade A. The role and place of medicinal plants in the strategies for disease prevention. Afr J Tradit Complement Altern Med. 2013 Aug 12;10(5):210-29. doi: 10.4314/ajtcam.v10i5.2. PMID: 24311829; PMCID: PMC3847409.
2. Miller LH, Good MF, Milon G. Malaria pathogenesis. Science. 1994 Jun 24;264(5167):1878-83. doi: 10.1126/science.8009217. PMID: 8009217.

3. Álvarez-Lario B, Macarrón-Vicente J. Uric acid and evolution. *Rheumatology (Oxford)*. 2010 Nov;49(11):2010-5. doi: 10.1093/rheumatology/keq204. Epub 2010 Jul 13. PMID: 20627967.
4. Gallego-Delgado, J., Ty, M., Orengo, J.M. *et al.* A Surprising Role for Uric Acid: The Inflammatory Malaria Response. *Curr Rheumatol Rep* **16**, 401 (2014). <https://doi.org/10.1007/s11926-013-0401-8>
5. Rao PV, Gan SH. Cinnamon: a multifaceted medicinal plant. *Evid Based Complement Alternat Med*. 2014;2014:642942. doi: 10.1155/2014/642942. Epub 2014 Apr 10. PMID: 24817901; PMCID: PMC4003790.
6. Yeti Nurhayati , Tresia Umarianti, Therapy of Cinnamon Decoction using Honey in Reducing Gout, *Indonesian Journal of Medicine* (2019), 4(1): 35-39, <https://doi.org/10.26911/theijmed.2019.04.01.06>.
7. Hanadi A. Attieh , Saleh Abu Lafi , Suhair Jaber , Qassem Abu-Remeleh , Pierre Lutgen and Mutaz Akkawi, Cinnamon bark water-infusion as an in-vitro inhibitor of β -hematin formation, *Journal of Medicinal Plants Research*, Vol. 9(38), pp. 998-1005, 10 October, 2015, DOI: 10.5897/JMPR2015.5931.
8. Parvazi S, Sadeghi S, Azadi M, Mohammadi M, Arjmand M, Vahabi F, Sadeghzadeh S, Zamani Z. The Effect of Aqueous Extract of Cinnamon on the Metabolome of *Plasmodium falciparum* Using (1)HNMR Spectroscopy. *J Trop Med*. 2016;2016:3174841. doi: 10.1155/2016/3174841. Epub 2016 Jan 20. Erratum in: *J Trop Med*. 2016;2016:9275636. PMID: 26904134; PMCID: PMC4745969.
9. Aggarwal BB, Yuan W, Li S, Gupta SC. Curcumin-free turmeric exhibits anti-inflammatory and anticancer activities: Identification of novel components of turmeric. *Mol Nutr Food Res*. 2013

Sep;57(9):1529-42. doi: 10.1002/mnfr.201200838. Epub 2013 Jul 12. PMID: 23847105.

10. Mustafa Kiyani M, Sohail MF, Shahnaz G, Rehman H, Akhtar MF, Nawaz I, Mahmood T, Manzoor M, Imran Bokhari SA. Evaluation of Turmeric Nanoparticles as Anti-Gout Agent: Modernization of a Traditional Drug. *Medicina*. 2019; 55(1):10. <https://doi.org/10.3390/medicina55010010>.
11. Raju C. Reddy, Palakkodu G. Vatsala, Venkateshwar G. Keshamouni, Govindarajan Padmanaban, Pundi N. Rangarajan, Curcumin for malaria therapy, *Biochemical and Biophysical Research Communications*, Volume 326, Issue 2, 2005, Pages 472-474, ISSN 0006 291X, <https://doi.org/10.1016/j.bbrc.2004.11.051>.
12. Büsing F, Hägele FA, Nas A, Döbert LV, Fricker A, Dörner E, Podlesny D, Aschoff J, Pöhl T, Schweiggert R, Fricke WF, Carle R, Bosy-Westphal A. High intake of orange juice and cola differently affects metabolic risk in healthy subjects. *Clin Nutr*. 2019 Apr;38(2):812-819. doi: 10.1016/j.clnu.2018.02.028. Epub 2018 Mar 3. PMID: 29571566.
13. Adumanya O. C. , Uwakwe A. A. , Odeghe O. B., Essien E. B. and Okere T. O. Assessment of the potency of some selected antimalaria drugs on the supplements of vitamin B2 and orange fruit juice (combination therapy), *African Journal of Biochemistry Research* Vol. 6(14), pp. 179-184, December 2012. DOI: 10.5897/AJBR12.034.
14. Shivraj Hariram Nile, Se Won Park, Chromatographic analysis, antioxidant, anti-inflammatory, and xanthine oxidase inhibitory activities of ginger extracts and its reference compounds, *Industrial Crops and Products*, Volume 70, 2015, Pages

238-244,ISSN 0926

6690,https://doi.org/10.1016/j.indcrop.2015.03.033.

15. Li J. [Forty-two cases of malaria treated with ginger-partitioned moxibustion in the Republic of Congo]. *Zhongguo Zhen Jiu*. 2011 Jun;31(6):559-61. Chinese. PMID: 21739708.
16. Hongjing Wang, Liping Cheng, Dingbo Lin, Zhaocheng Ma, Xiuxin Deng, Lemon fruits lower the blood uric acid levels in humans and mice, *Scientia Horticulturae*, Volume 220, 2017, Pages 4-10,ISSN 0304-4238,https://doi.org/10.1016/j.scienta.2017.03.023 .
17. Shija KM, Nondo RSO, Mloka D, Sangeda RZ, Bwire GM. Effects of lemon decoction on malaria parasite clearance and selected hematological parameters in *Plasmodium berghei* ANKA infected mice. *BMC Complement Med Ther*. 2020 Jan 30;20(1):24. doi: 10.1186/s12906-020-2820-1. PMID: 32020885; PMCID: PMC7076818.
18. Ramesh, Thiviyah (2021) A Comparison between the Phytochemicals of Apple Cider Vinegar and Pineapple Extract and Their Potential as Xanthine Oxidase Inhibitory Agent in Gout Treatment. Final Year Project (Bachelor), Tunku Abdul Rahman University College. <https://eprints.tarc.edu.my/19008/>.
19. <https://www.ndtv.com/health/world-malaria-day-2018-9-most-effective-home-remedies-for-malaria-1842256>.
20. Mehmood A, Zhao L, Ishaq M, Usman M, Zad OD, Hossain I, Raka RN, Naveed M, Zhao L, Wang C, Nadeem M. Uricosstatic and uricosuric effect of grapefruit juice in potassium oxonate-induced hyperuricemic mice. *J Food Biochem*. 2020 Jul;44(7):e13213. doi: 10.1111/jfbc.13213. Epub 2020 Apr 29. PMID: 32347580.

21. Olayemi, S.O., A.P. Arikawe, A. Akinyede, A.I. Oreagba and O. Awodele, 2012. Effect of malarial treatments on biochemical parameters and plasma pH of mice infected with *Plasmodium berghei*. Int. J. Pharmacol., 8: 549-554.

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