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A BRIEF REVIEW ON SINAPIC ACID

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ABSTRACT

Sinapic acid or sinapinic is a cinnamic acid derivative found in a variety of foods, edible plants, and fruits like broccoli, leafy brassicas and citrus juice. Its anxiolytic and anti-inflammatory propertieshave been studied and it is also known to be an effective antioxidant. Because of its free radical scavenging activity, it is able to inhibit the the production of hydroperoxide and peroxynitrite. Its antioxidant property has made it possible for improving various neuropathological conditions and improves cognitive dysfunction. Other activities like hepatoprotective, anticancer, antiproliferative, antihyperglycemic, anti-inflammatory, antimicrobial as well as antimycoplasmic have been reported.

INTRODUCTION

Sinapic acid is found abundantly in variety of foods, edible plants, and fruits like broccoli, leafy brassicas and citrus juice and known to have antioxidant property (1,2,3,4,5). Its protective effect against neuroronal death have been beneficial in treating ischaemia (6,7). Sinapic acid is an effective anxiolytic agent (8). Due to its free radical scavenging activity, it showed potent cardioprotective effects (9). Furthermore, it is a potent inhibitor of proin ammatory cytokine production (10). Its hepatoprotective activity was seen on arsenic induced toxicity in rats (11). It also exhibits antiproliferative as well as anticancer activity (12, 13). It is found to be a beneficial antihyperglycemic, antimicrobial and antimycoplasmic agent too (14, 15, 16).

CHEMISTRY

Sinapic acid (**Fig.1**) is a cinnamic acid derivative with two methoxy groups at the 3rd and 5th position (ortho and para) of the phenyl ring and a hydroxyl group at the 4th position (Meta) of the phenyl ring (2).

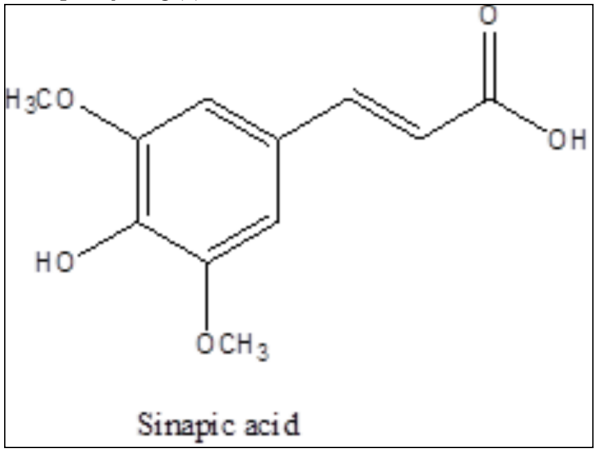

Figure 1: Sinapic Acid

The mechanism of action of sinapic acid towards OOH radicals can be explained by the transfer of hydrogen atom from its phenolic moiety whereas the mechanism towards OH, OCCl3 and OOCCl3 radicals was found to occur through a single electron transfer (5). The melting point of sinapic acid reported to be 192° C (17). Derivatives of sinapic acid isolated and identified are sinapine iodide (18), sinapine, (19) and sinapoyl glucose (20).

Pharmacological Activities

Neuroprotective Activity

A study on biochemical changes in the case of amyloid protein-induced Alzheimer's disease showed that sinapic acid can reduce the expression of nitric oxide synthase, glial cell activation as well as nitrotyrosine expression and improved neuronal cell death. (7). Studies such as kainic acid induced hippocampal brain damage in mice (21) and scopolamine-induced memory impairment in mice (22) postulated the potential neuroprotective effect of sinapic acid. Its memory improvement potency however was seen in *Polygala tenuifolia* extracts (23) and chinese medicinal herbs including *Poria cocos, Radix polygalae, Radix glycyrrhizae.* (24).

Anxiolytic Activity

Sinapic acid, a polyphenol present in *Lactuva sativa* is a potent anxiolytic agent (25) and its anxiolytic-like effects are mediated via GABA (A) receptors and potentiating Cl (-) currents (8).

Cardioprotective Activity

The protective effect of sinapic acid was seen in isoproterenol induced myocardial infarcted rats shown where biochemical changes such as an increase in serum creatine kinase and lysosomal lipid peroxidation and decrease in -glucuronidase and cathepsin-D was noted (26). Improved cardiac hypertrophy and electrocardiogram in these rats were also reported. (9).

Antioxidant And Free Radical Scavenging Activity

Sinapic acid found in wine showed antioxidant activity by inhibiting LDL oxidation in vitro which is the main step in the development of atherosclerosis (27). Sinapic acid when studied for its antioxidant activity along with ascorbic acid, kaempferol 3- O-rutinoside and *Tronchuda cabbage* extract, showed the strongest antioxidant activity (28).The antioxidant activity of lucerne extracts suggested that the presence of a ferulic acid and its related coumaric and sinapic acid might be responsible for its lipoxidase inhibitory action (29).

Anti-inflammatory Activity

Sinapic acid present in *Qingfei Xiaoyan Wan* showed anti inflammatory activity by significantly reducing the infiltration of cytokines and preventing other inflammatory pathways (30). Also, in case of CCl_4 induced acute hepatic injury in rats, liver histology showed reduced levels of serum alanine transaminase, aspartate transaminase and malondialdehyde. An inhibitory effect on inflammatory mediators and an increase in the expression of nuclear factor-kappa B was seen (10).

Hepatoprotective Activity

The ability to form metal chelators by sinapic acid has been postulated to be the mechanism for its protective role against arsenic induced toxicity in rats. Sinapic acid exhibit significant reversal of arsenic induced toxicity and an improved histopathological observation of the liver (11). In the case of Dimethylnitrosamine induced chronic liver injury in rats, sinapic acid inhibited body weight loss and exhibited increased levels of serum alanine transaminase, aspartate transaminase and liver malondialdehyde content. Formation of hepatic fibrosis was also prevented (31).

Antiproliferative And Anticancer Activity

Sinapic acid showed significant inhibition of Breast Cancer Resistance Protein (BCRP/ABCG2) which is an important factor in determining the absorption and disposition of consumed xenobiotics, various drugs and dietary phytochemicals (13). Based on the hypothesis that phenols can interfere with the proliferation or colony-forming ability of breast cells, sinapic acid was evaluated and reduced colony formation of breast cell was reported (32).

Other Activities

The antidiabetic activity of sinapic acid was observed in streptozocin-induced diabetic albino rats in which the biochemical parameters involved in hyperglycemia was brought to normal (14). Potential inhibitory effect towards the enzymes acetylcholinesterase and butyrylcholinesterase was also seen (33).

REFERENCES

1. Thiyam U, Stöckmann H, Zum Felde T, Schwarz K. Antioxidative effect of the main sinapic acid derivatives from rapeseed and mustard oil by-products. European Journal of Lipid Science and Technology. 2006 Mar;108(3):239-48..
2. Yun KJ, Koh DJ, Kim SH, Park SJ, Ryu JH, Kim DG, Lee JY, Lee KT. Anti-inflammatory effects of sinapic acid through the suppression of inducible nitric oxide synthase, cyclooxygase-2, and proinflammatory cytokines expressions via nuclear factor- B inactivation. Journal of agricultural and food chemistry. 2008 Nov 12;56(21):10265-72.
3. Zou Y, Kim AR, Kim JE, Choi JS, Chung HY. Peroxynitrite scavenging activity of sinapic acid (3, 5-dimethoxy-4-hydroxycinnamic acid) isolated from Brassica juncea. Journal of Agricultural and Food Chemistry. 2002 Oct 9;50(21):5884-90.
4. Natella F, Nardini M, Di Felice M, Scaccini C. Benzoic and cinnamic acid derivatives as antioxidants: Structure activity relation. Journal of agricultural and food chemistry. 1999 Apr 19;47(4):1453-9.
5. Galano A, Francisco-Márquez M, Alvarez-Idaboy JR. Mechanism and kinetics studies on the antioxidant activity of sinapinic acid. Physical Chemistry Chemical Physics. 2011;13(23):11199-205.
6. Lee HE, Kim DH, Park SJ, Kim JM, Lee YW, Jung JM, Lee CH, Hong JG, Liu X, Cai M, Park KJ. Neuroprotective effect of sinapic acid in a mouse model of amyloid β1–42 protein-induced Alzheimer's disease. Pharmacology Biochemistry and Behavior. 2012 Dec 1;103(2):260-6.
7. Kim YO, Lee SW, Oh MS, Lee HJ. Effects of sinapic Acid of 4 vessel occlusion model-induced ischemia and cognitive impairments in the rat. Clinical Psychopharmacology and Neuroscience. 2011 Aug;9(2):86.
8. Yoon BH, Jung JW, Lee JJ, Cho YW, Jang CG, Jin C, Oh TH, Ryu JH. Anxiolytic-like effects of sinapic acid in mice. Life sciences. 2007 Jun 27;81(3):234-40.
9. Roy SJ, Prince PS. Protective effects of sinapic acid on cardiac hypertrophy, dyslipidaemia and altered electrocardiogram in isoproterenol-induced myocardial infarcted rats. European journal of pharmacology. 2013 Jan 15; 699(1-3):213-8.
10. Shin DS, Kim KW, Chung HY, Yoon S, Moon JO. Effect of sinapic acid against carbon tetrachloride-induced acute hepatic injury in rats. Archives of Pharmacal Research. 2013 May 1;36(5):626-33.
11. Pari L, Jalaludeen AM. Protective role of sinapic acid against arsenic–Induced toxicity in rats. Chemico-biological interactions. 2011 Oct 15;194(1):40-7.
12. Kampa M, Alexaki VI, Notas G, Nifli AP, Nistikaki A, Hatzoglou A, Bakogeorgou E, Kouimtzoglou E, Blekas G, Boskou D, Gravanis A. Antiproliferative and apoptotic effects of selective phenolic acids on T47D human breast cancer cells: potential mechanisms of action. Breast Cancer Research. 2004 Apr 1; 6(2):R63.
13. Tan KW, Li Y, Paxton JW, Birch NP, Scheepens A. Identification of novel dietary phytochemicals inhibiting the efflux transporter breast cancer resistance protein (BCRP/ABCG2). Food chemistry. 2013 Jun 15;138(4):2267-74.
14. Kanchana G, Shyni WJ, Rajadurai M, Periasamy R. Evaluation of antihyperglycemic effect of sinapic acid in normal and streptozotocin-induced diabetes in albino rats. Global Journal of Pharmacology. 2011; 5(1): 33-9.
15. Misra LN, Wouatsa NV, Kumar S, Kumar RV, Tchoumbougnang F. Antibacterial, cytotoxic activities and chemical composition of fruits of two Cameroonian Zanthoxylum species. Journal of ethnopharmacology. 2013 Jun 21;148(1):74-80.
16. López A, De Tangil MS, Vega-Orellana O, Ramírez AS, Rico M. Phenolic constituents, antioxidant and preliminary antimycoplasmic activities of leaf skin and flowers of Aloe vera (L.) Burm. f. (syn. A. barbadensis Mill.) from the Canary Islands (Spain). Molecules. 2013 May;18(5):4942-54.
17. HOROWITZ RM, GENTILI B. Flavonoids of citrus. IV. Isolation of some aglycones from the lemon (Citrus limon). The Journal of Organic Chemistry. 1960 Dec;25(12):2183-7.
18. Kung HP, Huang WY. Chemical investigation of Draba nemorosa, L. The isolation of sinapine iodide. Journal of the American Chemical Society. 1949 May;71(5):1836-7.
19. Tzagoloff A. Metabolism of sinapine in mustard plants. I. Degradation of sinapine into sinapic acid & choline. Plant physiology. 1963 Mar;38(2):202.
20. Khattab R, Eskin M, Aliani M, Thiyam U. Determination of sinapic acid derivatives in canola extracts using high-performance liquid chromatography. Journal of the American Oil Chemists' Society. 2010 Feb; 87(2):147-55.
21. Kim DH, Yoon BH, Jung WY, Kim JM, Park SJ, Park DH, Huh Y, Park C, Cheong JH, Lee KT, Shin CY. Sinapic acid attenuates kainic acid-induced hippocampal neuronal damage in mice. Neuropharmacology. 2010 Jul 1;59(1-2):20-30.
22. Karakida F, Ikeya Y, Tsunakawa M, Yamaguchi T, Ikarashi Y, Takeda S, Aburada M. Cerebral protective and cognition-improving effects of sinapic acid in rodents. Biological and Pharmaceutical Bulletin. 2007;30(3):514-9.
23. Sun XL, Ito H, Masuoka T, Kamei C, Hatano T. Effect of Polygala tenuifolia root extract on scopolamine-induced impairment of rat spatial cognition in an eight-arm radial maze task. Biological and Pharmaceutical Bulletin. 2007 Sep 1;30(9):1727-31.
24. Lin Z, Gu J, Xiu J, Mi T, Dong J, Tiwari JK. Traditional chinese medicine for senile dementia. Evidence-Based Complementary and Alternative Medicine. 2012;2012.
25. Harsha SN, Anilakumar KR. Anxiolytic property of Lactuca sativa, effect on anxiety behaviour induced by novel food and height. Asian Pacific journal of tropical medicine. 2013 Jul 1;6(7):532-6.
26. Roy SJ, Prince PS. Protective effects of sinapic acid on lysosomal dysfunction in isoproterenol induced myocardial infarcted rats. Food and chemical toxicology. 2012 Nov 1;50(11):3984-9.
27. Satué-Gracia MT, Andrés-Lacueva C, Lamuela-Raventós RM, Frankel EN. Spanish sparkling wines (cavas) as inhibitors of in vitro human low-density lipoprotein oxidation. Journal of agricultural and food chemistry. 1999 Jun 14; 47(6):2198-202.
28. Sousa C, Valentão P, Ferreres F, Seabra RM, Andrade PB. Tronchuda cabbage (Brassica oleracea L. var. costata DC): scavenger of reactive nitrogen species. Journal of agricultural and food chemistry. 2008 Jun 11;56(11):4205-11.
29. Aziz AB, Grossman S, Budowski P, Ascarelli I, Bondi A. Antioxidant properties of lucerne extracts. Journal of the Science of Food and Agriculture. 1968 Oct; 19(10):605-8.
30. Cheng BF, Hou YY, Jiang M, Zhao ZY, Dong LY, Bai G. Anti-inflammatory mechanism of Qingfei Xiaoyan Wan studied with network pharmacology. Yao xue xue bao= Acta pharmaceutica Sinica. 2013 May;48(5):686-93.
31. Shin DS, Kim KW, Chung HY, Yoon S, Moon JO. Effect of sinapic acid against dimethylnitrosamine-induced hepatic fibrosis in rats. Archives of pharmacal research. 2013 May 1;36(5):608-18.
32. Hudson EA, Dinh PA, Kokubun T, Simmonds MS, Gescher A. Characterization of potentially chemopreventive phenols in extracts of brown rice that inhibit the growth of human breast and colon cancer cells. Cancer Epidemiology and Prevention Biomarkers. 2000 Nov 1;9(11):1163-70.
33. Szwajgier D, Borowiec K. Phenolic acids from malt are efficient acetylcholinesterase and butyrylcholinesterase inhibitors. Journal of the Institute of Brewing. 2012 Nov;118(1):40-8.