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A concise report on pharmacological and bioanalytical aspect of sinigrin

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ABSTRACT

Sinigrin (Allylglucosinolate) is precursors of the anticancer compounds allyl isothiocyanate which is found in *Brassica juncea, Phyllanthus emblica, Armoracia lapthifolia, Wasabia japonica* and some other plants. Except its uses as a medicinal compound it aslo have nutraceutical value. It protects plant from fungi, nematodes, plant pathogens and herbivores. Allyl isothiocyanate is produced from sinigrin through plant myrosinase or microbial myrosinase in gut microflora. Sinigrin have various type of pharmacological activity such as anticancer, antimicrobial and it suppresses NO production in the macrophages. This review will provide a brief idea about isolation techniques, analytical aspect and pharmacological activity of sinigrin. The data were collected from the available literature source in regards with sinigrin and it can be helpful to the researchers to get some idea about this unique phytoconstituents.

1. Introduction

Sinigrin, a major glucosinolate present in Indian mustard (*Brassica juncea* L.) seeds as the precursor of the anticancer compound allyl isothiocyanate[1]. Recently, it has been used as a nutrition supplement for their preventive and medicinal effect on some types of cancer and other diseases[2]. Cancer-protective compounds were found in the seeds of *Raphanus sativus* L. (glucoraphenin), *Sinapis alba* (sinalbin) and *Phyllanthus emblica* L. (sinigrin)[3]. Glucosinolates, or L-D-S-glucosides are widely distributed in cruciferous plants and play an important role in resistance to fungi, nematodes and other plant pathogens and herbivores. They may also serve to store inactive precursors of plant hormones such as 3-indolylacetic acid. The glucosinolate known as sinigrin (1-thio-L-D-glucopyranose 1-N- (sulfoxy)-3-buteneimidate is particularly abundant in *Armoracia lapthifolia* and *Wasabia japonica*[4]. Allyl isothiocyanate is produced from sinigrin, a glucosinolate contained in cruciferous vegetables, by plant myrosinase or microbial myrosinase in gut microflora. This isothiocyanate suppresses NO production and the induction of inducible nitric oxide synthase (iNOS) in LPS-activated J774 macrophages. Myrosinase is inactivated during cooking processes, such as boiling, steaming or baking, and cannot produce allyl isothiocyanate from sinigrin. Therefore, humans ingest mainly sinigrin, not allyl isothiocyanate, from cruciferous vegetable dishes after these cooking processes[5]. Seed and leaf tissue of *B. juncea* contain significant amount of sinigrin[6].

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2. Pharmacological activity of sinigrin

Allyl isothiocyanate, derived from the glucosinolate sinigrin is a well-recognized antimicrobial agent against a variety of organisms, including foodborne pathogens such as *Escherichia coli*[7]. Allyl isothiocyanate (AITC), which occurs in many common cruciferous vegetables, was stably stored as its glucosinolate precursor (sinigrin). Sinigrin itself was not bioactive, whereas hydrated form caused apoptosis and G(2)/M phase arrest in bladder cancer cell lines in vitro. In an orthotopic rat bladder cancer model, it inhibited bladder cancer growth and blocked muscle invasion[8]. Docking studies of enzyme and substrate was performed and illuminated the interactions of various active site residues with diverse groups of sinigrin[9]. The recombinant CpTGG1 expressed in *Pichia pastoris* catalyzed the hydrolysis of sinigrin and showing that CpTGG1 was indeed a functional myrosinase gene. Using sinigrin as substrate, the apparent K(m) and V(max) values of recombinant CpTGG1 were analysed and found to be significant[10]. Isothiocyanates have been implicated in the cancer-protective effects of brassica vegetables. When cabbage is consumed, sinigrin is hydrolysed by plant or microbial myrosinase partly to allyl isothiocyanate, which is mainly excreted as N-acetylcysteine conjugates of allyl isothiocyanate in urine[11]. Physiology of the gustatory receptor neurons (GRNs) in contact chemosensilla (insect gustatory organs) located on the antennae of the moth Heliothis virescens, emphasizing putative phagostimulants and deterrents. Sinigrin elicited responses in a larger proportion of gustatory receptor neurons (GRNs) than inositol, KCl, NaCl, and ethanol. Separate neurons showed excitatory responses to sinigrin[12]. In cabbage, glucosinolates such as sinigrin are hydrolyzed by plant myrosinase to allyl isothiocyanate, allyl cyanide in the presence of an epithiospecifier protein, 1-cyano-2,3-epithiopropane[13]. Sinigrin, the predominant aliphatic glucosinolate in cruciferous vegetables, is hydrolyzed to yield allylisothiocyanate, which, following absorption and metabolism in humans, is excreted in the urine as an N-acetyl-cysteine conjugate[14]. Electrophysiological recordings from the receptor neurons in sensilla chaetica during mechanical and chemical stimulation were performed, showing responses of one mechanosensory and of several gustatory receptor neurons[15]. Effect of sinigrin on carbohydrate and lipid metabolism in an animal rat model were investigated. The results showed sinigrin is multidirectional, indicating its impact on many organs like liver as well as pancreas and intestine[2]. Sinigrin also reduced the plasma triglyceride level, which suggests that alkenyl glucosinolates might be promising agents to prevent postprandial hypertriglyceridemia[16].

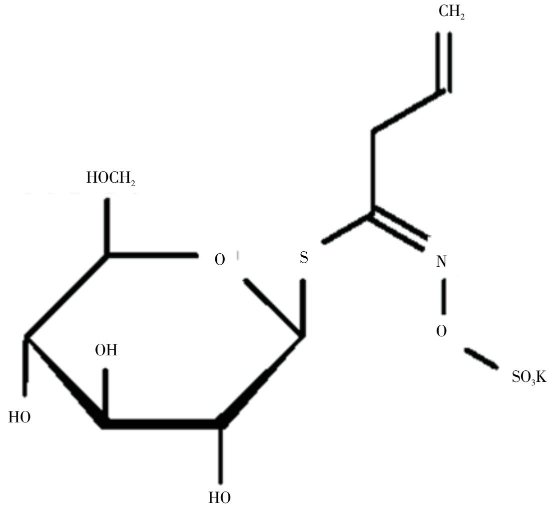

Figure 1. Chemical structure of sinigrin

3. Extraction and analytical technique of sinigrin

To investigate and optimize the factors affected the productivity of sinigrin in the process of extraction, response surface methodology were used. The ultrasonic-stimulated solvent extraction was suggested to be a promising method to improve the productivity of sinigrin[1]. A simple procedure for extracting and purifying sinigrin from Oriental mustard (Brassica juncea) meal using cold water was developed[17]. A hollow fiber microdialysis sampling coupled online to ion-pair liquid chromatography was investigated as an alternative to sample pretreatment for the direct determination of sinigrin in cruciferous vegetables without desulfation[18]. Near infrared diffuse reflectance spectroscopy method can be used to rapidly analyze the valid component in traditional Chinese medicine and in the quality control of sinigrin in different plant material[19]. Fruit extracts of Dithyrea wislizenii were analyzed for desulfoglucosinolates and intact glucosinolates using HPLC-APCI-MS and HPLC-ESI-MS, and found to have sinigrin as a active constituents[20]. Parent ion mapping is an analytical mass spectrometry approach that allows rapid assessment of glucosinolate content. Ion mapping proved to be highly sensitive and the glucosinolate sinigrin could be detected at three parts per trillion[21]. A reversed-phase HPLC method has been developed for determination of sinigrin in traditional Chinese plants. The samples were extracted with methanol and the extracts were cleaned on an activated Florisil column. A mobile phase gradient prepared from methanol and ammonium acetate at pH 5.0[22].

4. Tissue culture technique and ecological aspect of sinigrin

Interactive effects of Sand N supply on growth, seed yield, and the concentrations of glucosinolates and isothiocyanates in seeds were investigated and found that involvement of S-containing amino acids in both protein and glucosinolate synthesis. At intermediate S supply, a strong N-induced S limitation was apparent, resulting in high concentrations of sinigrin at low N supply only. Myrosinase activity in seeds increased under low N and low S supply[23]. Significant correlations between herbivore infestation rates and the presence or absence of sinigrin was presented. There was variation between herbivore species in the direction of response, the ecological scale at which responses were identified[24]. Presence of sinigrin in the diet of B. brassicae makes this aphid unsuitable as a food source for *Andraca bipunctata* but not for *Coccinella septempunctata*[25]. The higher level of sinigrin in wingless aphids had a significant negative impact on survival of a ladybird predator. Larvae of Adalia bipunctata were unable to survive when fed adult wingless aphids from a 1% sinigrin diet, but survived successfully when fed aphids from a glucosinolate-free diet[26]. The physiological and behavioural effects of sinigrin on the moth Heliothis virescens was investigated. The results suggested that sinigrin may act as negative reinforcers in H. virescens[27].

5. Discussion

Glucosinolates are a class of organic compounds that contain sulfur and nitrogen, and derived from glucose and an amino acid. They occur as a main phytoconstituent in different type of plant such as in Brassica juncea, *Phyllanthus emblica*, *Armoracia lapthifolia*, *Wasabia japonica* almost all plants. Glucosinolates play major roles in resistance to fungi, nematodes and other plant pathogens and herbivores and protect plant from these threats. Sinigrin, a major glucosinolate found in Brassica juncea was found to be as a precursor of the anticancer compound allyl isothiocyanate. This phytoconstituent have unique properties and have various type of pharmacological activity such as antimicrobial and anticancer activity. It can reduce the plasma triglyceride level. Various type of investigation have been done on sinigrin in regards with pharmacological activity, development of isolation and characterization process, development of analytical method and tissue culture technique to get higher percentage of sinigrin content. So all the above data presented in this review, could be usefull in the future for the development of new molecule for the treatment of various type of disease.

Conflict of interest statement

We declare that we have no conflict of interest.

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