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Review

Diversity, pharmacology and synthesis of bergenin and its derivatives: Potential materials for therapeutic usages

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ABSTRACT

Bergenin, a natural secondary metabolite, has been isolated from different parts of a number of plants. It is one of active ingredients in herbal and Ayurvedic formulations. It exhibits antiviral, antifungal, antitussive, antiplasmodial, antiinflammatory, antihepatotoxic, antiarrhythmic, anti-tumor, antiulcerogenic, antidiabetic and wound healing properties. It has been analyzed and estimated in different plant extracts, blood and drug samples using chromatographic techniques, and pharmacokinetic studies have been made. Several bergenin derivatives were isolated and/or synthesized and were found to possess pharmacological activities. Total synthesis of bergenin and its derivatives were reported. This review article covers literature on bergenin and its derivatives until 2013. Ethnomedicinal value of bergenin containing plant materials is also highlighted. This comprehensive review provides information on the potentiality of bergenin and its derivatives for therapeutic usages.

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Abbreviations: ABTS, 2,2′-azinobis-3-ethylbenzotiazoline-6-sulfonic acid; DCC, dicyclohexylcabodiimide; DEAD, diethyl azodicarboxylate; DIAD, diisopropyl azodicarboxylate; DMAP, N,N-dimethylamino pyridine; DME, 1,2-dimethoxyethane; DMF, N,N-dimethylformamide; DPPH, 2,2-diphenyl-1-picrylhydrazyl; EDC, ethyldimethylaminopropylcarbodiimide; IFN, interferon; IL, interleukin; MIC, minimum inhibitory concentration; PPTS, pyridinium p-toluenesulfonate; TBAF, tetra-n-butylammonium fluoride; TEMPO, 2,2,6,6-tetramethyl-1-piperidinyloxy free radical; Th, helper T cell; THF, tetrahydrofuran; TNF, tumor necrosis factor.

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1. Introduction of bergenin

Natural polyphenols of plant origin are often associated with medicinal values and are often used as intermediates for industrial products and pharmacological applications. Recent studies have proved that bergenin (**1**) (Fig. 1) possesses good pharmacological properties with low side effects and little toxicity. As indicated from the result of the ^{14}C-glucose incorporation experiment in *Saxifraga stolonifera* leaves, gallic acid is considered as the glucosyl acceptor for the biosynthesis of bergenin in nature [1]. Under continuous light, bergenin present in the young leaves showed the highest incorporation of label from ^{14}C-glucose and the addition of unlabeled gallic acid enhanced the incorporation label.

Bergenin (**1**) (also known as ardisic acid B, bergenit, bergenitol, cuscutin, peltophorin and vakerin) is a C-glucoside of 4-O-methyl gallic acid (2β-D-glucopyranosyl 4-O-methyl gallic acid δ lactone). It is an isocoumarin and hydrolysable tannin that obtain as a colorless crystal from MeOH. It has poor solubility in water and easily degrades in basic solution and its stability mostly depends on the storage conditions [2]. The initial structures of bergenin given by Tschitschibabin et al. (structure I) in 1928 [3] and Shimokôriyama (structure II) in 1950 [4] were revised by Hay et al. [5], Posternak et al. [6] and Fujise et al. [7] (Fig. 1). The structure of bergenin (**1**) was unequivocally confirmed through X-ray analysis of its 3,4,8,10,11-penta acetate derivative [8] and monohydrate [9,10].

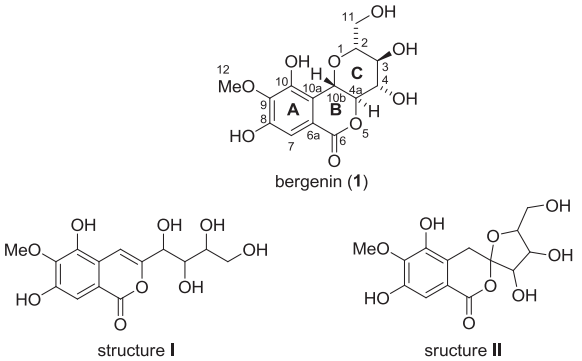

Fig. 1. Structure of bergenin.

2. Occurrence of bergenin in nature

According to citation in the Merck Index, bergenin (**1**) was first isolated from the rhizomes of *Saxifraga* (*Bergenia*) *siberica*