

REVIEW ARTICLE

Insight into the Isolation, Synthesis, and Structure-Activity Relationship of Piperine Derivatives for the Development of New Compounds: Recent Updates

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Abstract: Currently, black pepper commands the leading position among all the spices as a spice of great commercial importance in all the world trade and finds its way into the dietary habits of millions of people worldwide. Black pepper is biologically known as *Piper nigrum* and contains piperine as the main active chemical constituent. This paper highlights various general methods for extracting piperine from the crude drug such as maceration extraction, hydro-tropic extraction, accelerated solvent extraction, thin-layer chromatography, and extraction with ethanol & dichloromethane Ionic fluid-based ultrasonic-assisted extraction, *etc.* In this review, piperine and its analogs exhibit numerous pharmacological activities and synthetic schemes of insecticidal activity, anti-cancer activity, anti-inflammatory activity, anti-diabetic activity, anti-hyperlipidemic activity, antifungal activity, narcotic activity, *etc.*, and its structure-activity relationship. The biochemistry of piperine has also been summarized in the presented article. This very exhaustive review details the complete information about piperine, its derivatives, and further processing. Furthermore, the current study summarises recent research that has linked piperine to its use as a treatment for a variety of ailments.

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1. INTRODUCTION

Piperine (PIP) is a type of alkaloid isolated from black pepper (*Piper nigrum* Linn.). It belongs to the synthetic group of cinnamamides, which contract with the tranquilizer, hypnotics, anticonvulsant, and muscle relaxant activities [1]. The IUPAC name of piperine is (1-[5-[1,3-benzodioxol-5-yl]-1-oxo-2,4 pentadienyl]-piperidine. In 1820, piperine was first isolated by Hans Christian Oersted as a yellow semi-transparent strong alkaloid (Molecular weight = [285.33 g/mol-1], Melting point = [130°C]) inefficiently dissolved in water having weak base properties [2]. The most significant odorants present in *P. nigrum* are α -pinene, β -pinene, myrcene, a-phellandrene, limonene, linalool, methyl propanol, 2, 3-methyl butanal, butyric acid, and 3-methyl butyric acid [3]. Piperine has been recognized in a

few other plant-animal types (*Rhododendron faurie*, *Vicoa indica*, *Anethum Sowa*, and others). The filaments, starch, proteins, sugars, lignans, alkaloids, flavonoids, phenols, amides, and essential oils are present in black pepper [4]. The 1-piperoylpiperidine is synthetic piperine and a major bioactive fragment present in both black and white pepper [5]. Black pepper is known as "the King of Flavors" because of its strong aroma and highest yield based on worldwide trade volume [6]. Flavors are dietary constituents that enrich the taste of human food [7]. In recent research, piperine and its analogs have an anti-*Trypanosoma cruzi* action *in vitro*, and its molecules may have anti-trypanosomatid properties [8]. Piperine shows a contractile effect in the urinary bladder, which interferes through transient receptor potential vanilloid 1 (TRPV1) [9]. In conventional medicines, black pepper is used to treat epilepsy, migraines, and diabetes and as an antipyretic [10]. In Indian medication, piperine is utilized as an immune enhancer to treat against looseness of bowels, difficulty in breathing, persistent acid reflux, gastric afflictions, colic, sleep deprivation, and seizures [11]. The

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