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Piperine and curcumin as bioavailability enhancers for drugs

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Abstract

The chemical entities, which when mixed with drugs promote and augments their bioavailability without showing any synergistic effect with the drug are termed as bioenhancers [1]. The toxicity, cost, poor bioavailability and long term administration related to the drugs give rise to the need of bioenhancers which helps in overcoming most of the issues. They can be classified on the basis of their natural origin as well as on the various mechanisms attributed by them when applied in combination with drugs to improve their bioavailability. Herbal bioenhancers play a crucial role in enhancing the bioavailability and bioefficacy of different classes of drugs, such as antihypertensives, anticancer, antiviral, antitubercular and antifungal drugs at low doses [2]. Piper species produce a pungent alkaloid named Piperine or 1-peperoyl piperidine. Several herbal compounds including piperine, quercetin, genistein, naringin, sinomenine, curcumin, and glycyrrhizin have demonstrated capability to improve the pharmacokinetic parameters of several potent active pharmaceutical ingredients [3].

Piperine (1-piperoyl piperidine) is an amide alkaloid found in plants of Piperaceae family. The bioenhancing property of piperine was first utilized in the treatment of tuberculosis in human. Piperine was found to increase the bioavailability of rifampicin by about 60% and hence reduce the dose from 450 to 200mg [4]. In human medicine piperine is approved to be combined with anti-tubercular drugs. Piperine also showed enhanced bioavailability when combined with Nevirapine, a potent non-nucleoside inhibitor of HIV-1 reverse transcriptase which is used in combination with other antiretroviral agents for the treatment of HIV-1 infection [5]. Piperine also increases the bioavailability of curcumin, the active principle of Curcuma longa (turmeric). A 20 mg dose of piperine can increase the bioavailability of curcumin by 20 fold in humans. Several animal studies on piperine have shown promising results in bioenhancing capacity of piperine for various drugs [6, 7].

Turmeric (Curcuma longa) is a common household item used as remedy for various ailments. Curcumin is used as bioenhancer for antimicrobial agents and anticancer drugs. Curcumin, a flavonoid from turmeric suppresses drug metabolizing enzymes like CYP3A4 in liver and is also capable of inducing change in drug transporter P-gp and thus increased the bioavailability of celiprolol and midazolam in rats [8]. Curcumin suppresses UDP-glucuronyl transferase level in intestine and hepatic tissues [9]. It also modifies the physiological activity in the gastrointestinal tract leading to better absorption of drugs. Apart from traditional uses curcumin has proved to be an anti-inflammatory drug. Another mechanism reported that the bioavailability of drugs get enhanced due to the suppression of non-specific drug metabolizing enzyme by curcumin [10]

Bioavailability-enhancing activity of natural compounds may be attributed to several mechanisms of action. Different herbal bioenhancers may have same or different mechanisms of action. Nutritional bioenhancers enhance absorption by acting on gastrointestinal tract. Antimicrobial bioenhancers mostly act on drug metabolism processes.

Various mechanisms of action are proposed for bioenhancers which includes [11] (a) increase gastrointestinal absorption, (b) inhibition of solubilizer attachment, (c) Efflux of drugs from the site of action is reduced, (d) Reduced metabolism (e) bioenergetics and thermogenic properties. The mechanism of action has been shown in Fig.1 [2].

Many scientific studies and industries related to pharmaceutical products numerous are focusing on the improvement of bioavailability of a large number of potent drugs which are poorly bioavailable. The availability of natural bioenhancers provides an explorable route which in turn helps in reducing the dose of a drug and makes the cost of treatment economical and available to the broader section of the society.

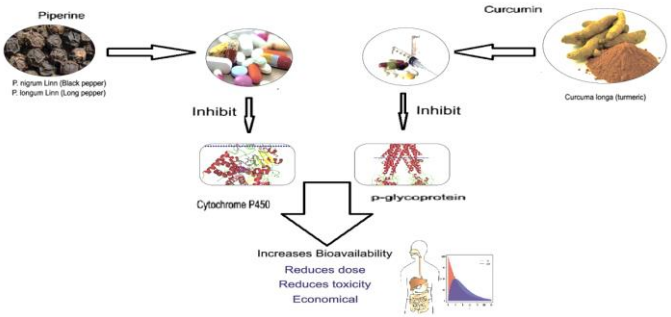

Fig 1: Mechanism of action of Piperine and Curcumin as Bioenhancers

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