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Novel Tablet Dosage Forms to Improve the Oral Bioavailability of Curcumin: A Short Review

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Abstract

Curcumin is a yellow pigment that is considered as the major biologically active compound of turmeric plant. Curcumin has antioxidant, anti-inflammatory, anti-microbial, anti-neoplastic, and anti-depressant properties. However, due to poor oral bioavailability, its applications has been largely hampered in the clinical settings. Currently, advances in curcumin formulations to different dosage forms such as tablets, capsules or semisolid preparations have been resulted in solving its poor oral bioavailability and subsequently increasing the blood levels of drug for therapeutic activity. In this article, the ongoing researches of formulation of curcumin into different dosage forms that have been used to improve its oral bioavailability has reviewed. In particular, we have focused on formulation of curcumin into tablet dosage forms because the tablet is the most popular type of dosage form for the patients.

Keywords: Curcumin, bioavailability, liquisolid tablets, floating tablets, mucoadhesive tablets and nanoemulsion tablets.

1. Introduction

Curcumin is a polyphenolic compound that is the major biologically active constituent in the turmeric (Curcuma longa L, family Zingiberaceae). It is lipophilic compound with a low solubility and stability in aqueous solution [1]. Commercially available curcumin is consisted of diferuloylmethane (77%), dimethyl curcumin (17%) and bisdemethoxy curcumin (6%) [2]. Curcumin has known as relatively low toxicity to human and animals. Therefore, it is generally regarded as safe compound by the Federal Food, Drug, and Cosmetics Act of US FDA [1].

2. Uses of curcumin

Through the past decade, curcumin has been used for many therapeutic and nontherapeutic purposes by the human beings. Many studies have shown that curcumin possess considerable efficacy in preventing and treating various diseases and illnesses [3]. For instance, it exerts a wide range of beneficial therapeutic activities, including antioxidant, anti-inflammatory, anti-microbial, anti-neoplastic, metabolism regulating and anti-depressant effects. It has been used for the treatment of jaundice, menstrual difficulties, hematuria, hemorrhage, and colic [3,4].

Besides using for the pharmacological benefits, curcumin has been used in cooking materials as flavor and color in Asia. Curcumin has also been used in cosmetic and it is an official in China as well as in another Asian countries [5].

3. Oral bioavailability of curcumin

Curcumin is familiar to have a poor bioavailability after oral administration, which affects negatively and its therapeutic activity. The reason for low bioavailability of curcumin is due to a poor absorption, high metabolic, elimination rate and inactivity of its metabolites [6]. Gupta and his co-worker evaluated the oral bioavailability of curcumin and they found that even after a single oral dose of 12 g of curcumin, it was rarely detected in human plasma. They were related the low bioavailability of curcumin to low solubility in aqueous gastrointestinal fluids, low chemical stability at physiological pH, low absorption in the gastrointestinal tract (GIT) and rapid metabolism in the GIT and liver [7].

4. Mechanism of action of curcumin

Curcumin exerts its pharmacological activity through different mechanisms of actions. For instance, it exhibits a strong antioxidant activity through increasing the cellular resistance to oxidative damage as well as its ability to reduce the formation of proinflammatory cytokines. It is recognized that curcumin has stronger antioxidant effect as compare to vitamins C and E [3,8].

Curcumin administration significantly is reduced liver injury in tested animals compared to control animal groups. Also, curcumin is inhibited

fungal aflatoxin production by 90% in addition to the role of turmeric and curcumin in reversing biliary hyperplasia, fatty changes and necrosis. The studies shows that the turmeric have role in treatment of diabetes, gastrointestinal disorders and neurological diseases through different mechanisms of actions [9,10]. Turmeric, is the main source of curcumin, may also be applied topically to counteract the inflammation, an irritation associated with inflammatory skin conditions and allergies. Curcumin is able to inhibit carcinogenesis at the three stages: tumour promotion, angiogenesis and tumour growth [9,10].

5. Types of curcumin tablets

5.1. Curcumin floating tablets

Floating tablets have an initial low density so they can float immediately in GIT media without lag time. In recent years, floating tablets have become attractive and increasingly used as a gastroretentive dosage form. This is because floating tablet can prolong the gastric retention time and improve drug bioavailability. For formulation of floating tablets, low density materials such as polypropylene foam powder and many others can be used [6] (Fig. 1).

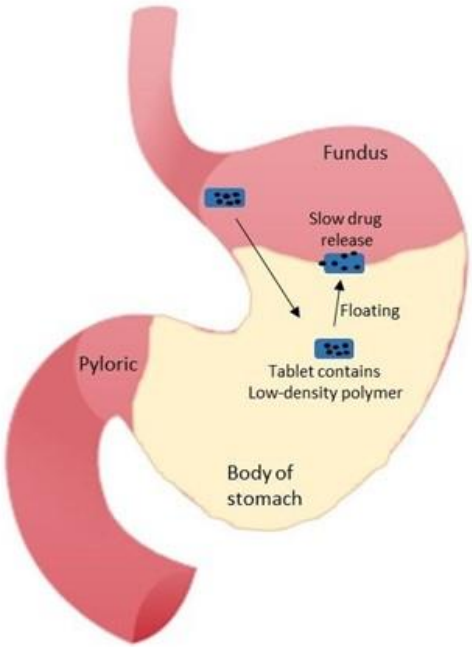

Fig.1. Diagram illustrates the floating mechanism of floating tablets containing low density excipient (s) in GIT media (stomach).

Curcumin can be formulated as a floating tablet because it can be able to stand in acidic conditions without a degradation [6]. The floating tablets of curcumin are usually prepared by using a direct compression method. Forinstance in a study, curcumin tablet is prepared using hydoxypropyl methylcellulose (HPMC) and polypropylene foam powder. Curcumin, HPMC and other ingredients are thoroughly mixed and compressed into tablets. The obtained results show that incorporation of HPMC into tablets formulation could provide immediate floatation upon contact with the dissolution medium without lag time. Additionally, the floating tablets are able

to control drug release over a period of 8 h as compared to all other formulations [11].

In another study, curcumin floating tablet is also prepared using hydroxypropyl methylcellulose, dicalcium phosphate, sodium carbonate, citric acid and carbopol. Upon evaluation of the tablet, it exhibited maximum sustained release of curcumin with excellent floating and swelling properties. Also, in vivo antitumor studies confirm that the overall rate of tumor incidence and number of tumors is less in mouse's group treated with floating tablet compared to control animal groups [12].

5.2. Curcumin mucoadhesive buccal tablets

Currently, there is an increasing interest of the buccal route of drug administration as compared to other routes for both local and systemic effects. This might be due to the thin mucosal layer of the oral cavity, which produce a rich blood supply and lymphatic drainage, leading to higher bioavailability, because the drug is directly drained into the systemic circulation, avoiding the first pass metabolism, drugs with high toxicity cannot be used [13].

For instance, mucoadhesive buccal tablets can increase residence time, subsequently facilitate absorption by adhesion to cellular surface and hence improve bioavailability [13,14]. The mucoadhesion means that the use of some materials such as certain types of polymers to bind the mucin layer. The polymers used for mucoadhesion should fulfill certain physiochemical properties such as having suitable surface tension to wet the mucosal layer, suitable flexibility in order to penetrate the mucosal layer and should possess bio-adhesive properties.

Mucoadhesive buccal tablets are present as small and flat tablets, so they can be held in the buccal pouch between gum and cheek. They may be designed to release the drug immediately or slowly for an extended action. Mucoadhesive buccal tablets can be manufactured by compression methods or wet granulation. Moreover, sometime the multilayered tables are formed in order to ensure unilateral release of drug, this is done by adding and compressing ingredients layer by layer with a hydrophobic polymer as a packing membrane [15].

In a previous study, mucoadhesive tablets of curcumin were successfully prepared by direct compression using chitosan as a hydrophilic mucoadhesive polymer. Because of its non-toxic, biodegradable and biocompatible characteristics, chitosan was drawn attention to be used as a mucoadhesive polymer. In addition, the paracellular transport of drug can be facilitated by its strong mucoadhesive property along with its interaction with tight junction, by opening the tight junction of the mucosal barrier. In this study, curcumin bioadhesive tablets were found to have

the advantage of bypassing the first-pass metabolism, hence increasing bioavailability. In addition, the increased patient acceptance compared with injections and compared to oral route there is relatively rapid onset of action [16].

5.3. Curcumin liquisolid tablets

Liquisolid system can be defined as a novel concept of drug delivery that is used for the oral drug delivery. Water insoluble and lipophilic drugs, such as curcumin can be released in sustained manner from the liquisolid systems. The tablet manufacturing method of liquisolid tablets is a simple process, consisting of preparation of a mixture by dissolving the drug in a suitable non-volatile solvent and adding the liquid drug to a carrier and coating material mixture. The resulting liquisolid mixture then compressing into a tablet using suitable tablet machine.

Poorly water soluble drugs such as curcumin have low dissolution rate, hence, to improving their bioavailability, they can be formulated as liquisolid tablets. In liquisolid tablets formulation technique, a powder with acceptable flow and compression properties can be obtained on liquid medications such as solutions or suspensions. The liquisolid technology is one of the most promising methods of improving the dissolution rate of poorly soluble drugs because it is simple cost-effective and commercial attractive for industrial manufacturing [17].

There are numerous advantages for formulating curcumin as a liquisolid tablet, such as increasing the permeability in acidic conditions, blocking the P-glycoprotein activity and inhibiting the multidrug resistance protein. All these advantages can be used to significantly improving the poor solubility and bioavailability of curcumin [18].

5.4. Curcumin nanoemulsion tablets

Nanotechnology is an emerging field that is widely used in medical and pharmaceutical applications. Enhancing the bioavailability of curcumin by nanoparticle formulations was a widely reported in literatures. Curcumin nanoparticle in an emulsion form is higher than the normal curcumin form in solubility and absorption rate, and hence has a better bioavailability. Various tablet dosage forms can be prepared from nanoemulsion. However, transforming curcumin nanoemulsion into a tablet dosage form of course is complicated process. This is because of the compression force which can damage the structure of the nanoemulsion and loss it. Therefore, careful selection on the tablet composition and process are the important steps in this formulation. On the top of that, the filler will contribute mainly on the successful tableting, to evaluate the potential of the filler in the tableting of curcumin nanoemulsion, several parameters were performed. The observation of nanoemulsion

morphology and particle size after tableting were important parameters which will tell the successful transformation from nanoemulsion to tablet [19].

One example of the preparation of curcumin in nanoemulsion is the using of self-nanoemulsification (SNE) technique. During the preparation of curcumin nanoemulsion, oil-glyceryl monooleate, surfactant-cremophor, co-surfactant-PEG400 in a certain ratio were mixed to form the oil phase. Then, the mixture was placed in sonicator bath at room temperature to completely homogenizing the mixture. Subsequently, the SNE formed was added with water by which the ratio of SNE: deionized water was 2: 1 and proceed with stirring for certain period. A clear, homogenous nanoemulsion was obtained in this study which can be further used in tablet dosage forms [19].

6. Conclusions

Despite of using of curcumin in various fields of medicine, it is hard to find a direct application way this is due to its low oral bioavailability. Various methods have been successfully developed to increase the bioavailability such as tablet dosage forms and still it is necessary to find out that the best suitable method which is effective and economical. In the past decades, there are different types of curcumin tablets such as floating tablets, mucoadhesive buccal tablets, liquisolid tablets and nanoemulsion tablets were successfully developed. However, these curcumin tablets still need a vigorous bioavailability study in vitro and in vivo. This is definitely to ensure that the tablet formulation of curcumin is better than another types of dosage forms in enhancing the bioavailability.

Conflict of interest

The authors declare no competing financial interest.

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