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Preparation, characterization and anti-colitis activity of curcumin-asafoetida complex encapsulated in turmeric nanofiber

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ABSTRACT

Ulcerative colitis (UC) is a main form of inflammatory bowel disease (IBD). Asafoetida (ASF) and turmeric have traditionally been used for the treatment of various inflammatory diseases, including UC, because ASF is rich in sulfur compounds and turmeric contains curcumin (CUR). Turmeric nanofiber (TNF), the modified cell wall component of turmeric is considered to play important role in the human diet, health and can be used as a carrier agent to encapsulate bioactive components. A novel gut health product (GHP) was formulated by encapsulation of ASF and CUR complex onto TNF. The GHP was characterized by UPLC, GC-MS, FTIR, XRD, SEM with EDS and DSC studies. GHP was evaluated for anti-colitis activity in a rat model of 5% dextran sulfate sodium (DSS) induced UC. Treatment with GHP significantly attenuated the disease activity index, colitis score, histopathological changes and myeloperoxidase activity. GHP has significant protective effects against DSS induced colitis.

1. Introduction

Gut health is a complex concept and it is proposed as three most important components, namely the diet, the mucosa, and the commensal flora. The mucosa is composed of the digestive epithelium, the gut-associated lymphoid tissue and the mucus overlying the epithelium. The gut-associated lymphoid tissue, commensal bacteria, mucus and host epithelial cells interact with each other, forming a delicate and dynamic equilibrium within the alimentary tract that ensures efficient functioning of the digestive system [1]. Ulcerative colitis (UC), which is the main form of inflammatory bowel disease (IBD), is a nonspecific inflammatory disease of the large intestine. In addition, it is a lifetime illness with intense emotional and social impacts, it causes severe intestinal tract damage and its development to chronic UC can lead to colon cancer [2,3].

Food and feed should be selected to favor conditions in the gut that create and stabilize this equilibrium between the host, the micro flora, and environment, and to prevent trouble of the structure and function of the gut [1]. Dietary fiber (DF) has a marked effect on gut anatomy, gut development and gut function. DF is the main substrate for bacterial fermentation, particularly in the large intestine of human and also non-ruminant animals. As DF interacts both with the mucosa and the microflora, it has an important role in the control of gut health. In general, DF ingestion leads to the increased size and length of the digestive organs, including the small intestine, caecum and colon [4,5]. These effects are often associated with modification of the gut epithelium morphology, and consequently with the hydrolytic and absorptive functions of the epithelium. Mucins are the major glycoproteins of the mucus layer that coats and protects the gut from infection, and from physical, chemical and enzymatic injuries, and aids the passage of lumen contents through the tract. DF increases the excretion of mucin at the terminal ileum in many species, including the pig, rat and man. DF modulates gut health by way of complex interactions with the gut epithelium, the mucus and the micro flora [1].

DF is a broad category of non-digestible cell wall component of plant materials that includes non-starch polysaccharides, oligosaccharides, lignin, and analogous polysaccharides with an associated health benefit [6]. The physical properties of DF vary, and even a slight variance may influence the physiological effect of the DF. DF is classified by solubility in water, viscosity and microbial fermentation in the large intestine. Soluble DFs include pectin, gums, and polysaccharides, whereas insoluble DFs include cellulose, hemicellulose and lignin [7]. Many studies suggest that there is an association between high DF intake and a low incidence of colon cancer by reducing the digestion,

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absorption of macronutrients and decreasing the contact time of carcinogens within the intestinal lumen [6,8,9] and that DF has anticancer properties [6,10,11]. Furthermore, the US Food and Drug Administration have approved health claims supporting the role of DF in cancer prevention [12]. DF increases fecal bulking and viscosity, reduces the time for proteolytic fermentation that results in harmful substances, and shortens the contact between potential carcinogens and mucosal cells. In addition, DF can bind/excrete potential luminal carcinogens, lower fecal pH in the colon, and thus provides a healthy intestinal environment. DF decreases the risk for type 2 diabetes mellitus, obesity, cardiovascular disease, colon cancer, and improves immunity by modulating the gut microbiota landscape [6]. DF modulates our health at nearly every level, and in every organ system, through complicated modes of action, many of which remain to be determined. DF bind potential nutrients, result in new metabolites, and modulate nutrient absorption/metabolism. DF consumption can have significant health benefits, particularly in laxation, mineral absorption, potential anticancer properties, lipid metabolism and anti-inflammatory effects [11].

Turmeric is well known for its medicinal properties and most of the medicinal properties of turmeric have been reported to be due to the active principle curcuminoids viz. curcumin, demethoxycurcumin and bisdemethoxycurcumin which were found to be beneficial in improving many biological activities [13]. However, not much is known about the various applications of turmeric when curcuminoids are removed from the turmeric. The extracted curcumin from turmeric markets as a value added nutraceutical and the material that remains is a by-product called turmeric spent. This turmeric spent is rich in dietary fiber (45%) contains both soluble (2%) and insoluble (43%) fibers. Nanofibers (NF) and dietary fibers (DF) are well established to play a beneficial role against various diseases like diabetes, gastrointestinal disorders, colon cancer, heart disease, etc. [14,15]. A number of research reports are available showing the development of nanofibers and blending through wide range of biodegradable natural or synthetic polymers loaded with bioactive molecules for their potential applications [16,17], such as tissue engineering [18–21], wound dressing [22], drug delivery [23] and medical devices [16,24,25]. NF prepared from biomaterial, turmeric spent containing DF is called as turmeric nanofiber (TNF) can be utilized to improve gut health as well as used as an encapsulating agent of natural bioactive compounds for the treatment of a wide range of pharmacological activities particularly gastrointestinal health and anti-colon cancer.

Natural health products as functional foods are currently being investigated on a priority basis for potential health promotion and reduction of disease risks. Current research trends have focused on the encapsulation of bioactive compounds or bioactive natural extracts into nanofibers as composites. Encapsulation is widely used in the food, chemical and pharmaceutical industry to develop new functional foods or formulations containing or incorporating bioactive phytochemicals and plant extracts to enhance food safety and promote health. It is used to protect active molecules against light, humidity and oxygen in order to avoid or delay their degradation and stabilize them during storage before use. It also allows limiting or controlling their transfer to the environment in order to avoid losses, to mask some of their properties such as taste, odor, catalytic activity or to get a controlled release at given time and place; and total or progressive dosed delivery [26].

Asafoetida (ASF) – [*Ferula asafoetida*] is an oleo-gum-resin and used as a flavoring agent in food and as a traditional medicine for many diseases in many parts of the world. It has a strong, tenacious and sulfurous odor and it is a popular ingredient in the Indian cuisine, most probably because its odor is reminiscent of the flavor of garlic and onion, two sprouting vegetables, as well as meat. ASF is traditionally used for the treatment of different diseases, such as whooping cough, asthma, ulcer, epilepsy, stomachache, flatulence, bronchitis, intestinal parasites, antispasmodic, weak digestion and influenza [27]. ASF is an effective remedy for several diseases of the stomach. The digestive stimulant actions of ASF are the most commonly experimented beneficial physiological effect via enhanced secretion of saliva and activity of salivary amylase. It plays an important role in the digestion of dietary lipids by stimulating bile flow and enhances the bile acid secretion and also enhances the activities of digestive enzymes of the pancreas and small intestine. Moreover, it is used for low acid levels in the stomach, stomach pressure, flatulence and loose stools. Recent pharmacological and biological studies have also been reviewed and shown several activities, such as antioxidant, antimicrobial, antiviral, antifungal, cancer chemopreventive, anti-diabetic, anticarcinogenesis, antispasmodic and hypotensive, relaxant effect, neuroprotective and molluscicidal from this ASF [27]. ASF consists of three main fractions; including resin (40–64%), gum (25%) and essential oil (10–17%) [28]. The resin fraction contains coumarins, sesquiterpene coumarins, ferulic acid and its esters and other terpenoids. The gum includes glucose, galactose, 1-arabinose, rhamnose, glucuronic acid, polysaccharides and glycoproteins, and the volatile fraction contains sulfur-containing compounds, monoterpenes and other volatile terpenoids. Sulfur compounds in *F. asafoetida* resin show various biological activities and can be valuable in medicine [27].

Curcumin (CUR) [diferuloyl methane] is naturally occurring flavonoid compound found in the plant *Curcuma longa* which is used as food additives and have been shown to possess a wide range of biological and pharmacological activities such as anti-inflammatory, anticancer, antioxidant, antimicrobial, neuroprotective, cardioprotective and radio-protective effects [13]. CUR strongly inhibits proliferation of HT-29 and HCT-15 human colon cancer cell lines [29].

TNF, ASF and CUR have been linked with gut health by beneficial effects in gastrointestinal inflammatory disorders and protection from colon cancer. In this regards on the basis of their safety, nutritional value and bio-pharmacological importance our research group designed and developed a formulation to improve gut health. The best of our knowledge, no study has been reported so far in the available literature describing ASF and CUR jointly encapsulated with TNF using spray drying technique. In the present study reports for the first time the design of gut health product (GHP) formulation by encapsulating ASF and CUR onto TNF. The GHP was characterized by SEM with EDS, IR, XRD and DSC studies. The study was also carried out to evaluate the anti-colitis effect of gut health product in dextran sulfate sodium (DSS) induced colitis in rats.

2. Materials and methods

2.1. Materials and chemicals

Turmeric residues (after extraction of the active chemical constituents), ASF oleoresin and CUR (95%) were collected from Plant Lipids (P) Ltd., Kerala, India. The turmeric residues were cleaned thoroughly with running tap water followed by soaking in double distilled water and dried. Quillaja saponin (Q-Naturale® 200) was purchased from Ingredion India Pvt. Ltd., Mumbai, India. All the chemicals used in the present study viz. sodium chlorite, acetic acid, dextran sulfate sodium (DSS) (MW = 36,000–50,000), hexadecyltrimethylammonium bromide, hydrogen peroxide, O-dianisidine dihydrochloride and disodium hydrogen phosphate were analytical grade and purchased from Sigma Aldrich, Mumbai, India.

2.2. Physical parameters

2.2.1. Bulk density

Bulk density (g/mL) of TNF and GHP was determined by adding 10 g of sample into an empty 100 mL graduated cylinder and place the cylinder on a ring stand and adjust the ring clamp so that, when the base of the cylinder is raised to touch the ring, the bottom surface of the cylinder is exactly one inch from the base of the ring stand. The ratio of mass of the sample and the volume occupied in the cylinder determines the bulk density values [30].