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Okra extracts in pharmaceutical and food applications

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ABSTRACT

The potential of okra extract was evaluated for uses in pharmaceutical and food applications. Okra polysaccharides were extracted and dried using different drying procedures (oven drying and freeze-drying). The extracts were examined by means of measurement of swelling and dissolution behaviour of okra extract-based hydrophilic matrices for controlled drug release and emulsification capacity of *n*-hexadecane. Drying technique and solubility of drugs used were shown to have a significant impact on the swelling and dissolution of the hydrophilic matrix tablets prepared. It was shown that the oven-dried extracts increased swelling of the matrices by approximately 20% compared with freeze dried extracts, resulting in slower drug release. The relative drug solubility also contributed to the extent of swelling and drug release with poorly soluble flurbiprofen reducing the swelling and the release rate when compared with freely soluble theophylline. The emulsification capacity of the okra extracts was also investigated and they were found to emulsify *n*-hexadecane at pH 3.0. The emulsions produced had an average droplet size of ~6 μm rising to ~23 μm after 5 days then remaining relatively constant following 30 days of storage. These results highlight the potential of okra polysaccharide as an alternative sources to fabricate hydrophilic matrix tablets or as stabilisers of emulsions that can be used to deliver drugs or nutrients.

1. Introduction

Okra (*Abelmoschus esculentus* L.) is a plant which is widely cultivated in the tropics, sub-tropics and warm, temperate regions around the world including Africa, Asia and North America with total trade estimated to over $5 billion (FAO, 2013). Okra extracts obtained from fresh okra pod, are naturally available, inexpensive and non-toxic biopolymers, which make okra an attractive resource for industrial applications. The polysaccharides within okra extracts are predominately pectins. Pectins are acidic heteropolysaccharides consisting of three segments, namely homogalacturonan (HG), rhamnogalacturonan I (RG-I) and rhamnogalacturonan II (RG-II) regions (Willats, Knox, & Mikkelsen, 2006). Homogalacturonan (HG) is mainly composed of α-(1 → 4) linked α-D-galacturonic acid (GalA) residues containing methyl esterified carboxyl groups and partially acetylated hydroxyl groups at *O*-2 and/or *O*-3 positions. RG-I branches consist of repeating units of α-(1 → 4) linked α-D-galacturonic acid and α-(1 → 2) linked α-L-rhamnose. Rhamnose residues of RG-I regions may also contain arabinan, galactan and/or arabinogalactan side chains at rhamnose 4-*O* positions (Vincken et al., 2003). The RG-II domain has a backbone similar to previous units but its structure is more complex due to the presence of a diverse range of sugar monomers (Willats et al., 2006). Like many other biopolymers, the physicochemical properties of okra polysaccharides are amenable to interdisciplinary applications between the pharmaceutical and food industry in both dry and hydrated systems.

Hydrophilic matrix tablets are the most frequently employed oral drug delivery devices for controlled drug release applications (Ghori, Ginting, Smith, & Conway, 2014; Wen, Ali, & Rajabi-siahboomi, 2010). Furthermore, the use of naturally resourced biopolymers has gained considerable attention in the last few decades, as they have the potential to be utilised in the wide range of pharmaceutical formulations including matrix tablets, topical gels and emulsions (Rana et al., 2011). Owing to their cost effectiveness, availability and good regulatory acceptance they have the ability to compete with the semi-synthetic and synthetic polymers in the market (Wadhwa, Nair, & Kumria, 2013). A number of natural and modified polysaccharides, such as xanthan gum (Jian, Zhu, Zhang, Sun, & Jiang, 2012), guar gum (Dürig & Fassihi, 2002), grewia gum

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(Nep & Conway, 2011a), karaya gum (Munday & Cox, 2000), alginates (Holte, Onsøyen, Myrvold, & Karlsen, 2003) or carrageenan (Picker, 1999) have shown to be useful for controlled-release tablet formulations due to their hydrophilic properties. Okra performance in tableting it is similar to other commercially available polysaccharides and a relatively simple extraction procedure and abundant nature however, make it an attractive alternative (Zaharuddin, Noordin, & Kadivar, 2014)These polymers swell when they contact with liquid, forming a gel layer across the tablet surface through which drug is liberated (Bhardwaj, Kanwar, Lal, & Gupta, 2000; Wen et al., 2010). Okra extract attributes are ample enough to warrant its investigation as a hydrophilic polymer in controlled-release drug delivery systems or as a carrier of pharmaceutical ingredients for oral extended release formulations (Emeje et al., 2010; Kalu, Odeniyi, & Jaiyeoba, 2007). Furthermore, they have also shown good emulsion stabilising properties in acidic environments with potential applications in fruit drinks or acidified dairy products (Alba, Ritzoulis, Georgiadis, & Kontogiorgos, 2013; Kontogiorgos, Margelou, Georgiadis, & Ritzoulis, 2012; Ndjouenkeu, Akingbala, & Oguntimein, 1997; Ndjouenkeu, Goycoolea, Morris, & Akingbala, 1996). The rate of drug release from different biopolymers is influenced by the relative contribution and interplay between swelling and dissolution processes as well as the emulsification capacity. However, such functional properties are controlled by the extraction protocol that influences the backbone composition of the extracted biopolymer.

The aims of the present investigation, therefore, were to study the functional properties of polysaccharides extracted from okra obtained at pH 6.0 in food and pharmaceutical applications. To this end, swelling and dissolution properties of hydrophilic matrix tablets and emulsifying capacity were studied. Two model drugs were used in the studies, one with low aqueous solubility, flurbiprofen (8.0 mg/L), and one with moderate solubility (theophylline, 7.3 g/L) (Yalkowsky, He, & Jain, 2010).

2. Materials and methods

2.1. Materials

Fresh okra pods were purchased from local market and were frozen and kept at −20 °C until handling. Flurbiprofen (FBP) and theophylline (THP) were purchased from Aesica Pharmaceuticals Ltd (Cramlington, UK) and Tokyo Chemical Industry Ltd (UK), respectively. Citric acid monohydrate, sodium citrate dehydrate were used for citric buffer preparation, sodium azide was used as a preservative and *n*-hexadecane as dispersed phase for o/w emulsions. All reagents were obtained from Sigma–Aldrich (UK). Disodium hydrogen phosphate (Na_2HPO_4) and sodium dihydrogen phosphate (NaH_2PO_4) were purchased from Fisher Scientific, (UK). All reagents used were analytical grade.

2.2. Isolation of okra extracts

Extraction of okra polysaccharides was performed at pH 6.0 and the procedure is described elsewhere in detail (Alba et al., 2013). Briefly, seeds and calyces were removed and the remaining parts of the pods were blended. Extraction of polysaccharides was performed at pH 6.0 at 70 °C. Insoluble particles were removed by centrifugation and the polysaccharides were precipitated with organic solvent (alcohol or acetone). An aliquot of the precipitate was freeze-dried and is referred to as FDOG. The other part was oven-dried at 40 °C for 24 h (designated as ODOG). Following this the okra extracts were ground to 250 μm, and then sieved to 150–250 μm particle size fraction.

2.3. Powder blending

Powder mixtures of okra extracts with flurbiprofen (FBP) and theophylline (THP) were prepared at a fixed extract to drug ratio of 25% and 50%. The samples were tumble mixed for 20 min (50 rpm) and a random sample of 10 mg was taken from each powder mixture to evaluate the content homogeneity. Drug content was determined using UV–Vis spectrophotometry at a maximum wavelength (λ_{max}) of 247 or 272 nm for FBP and THP, respectively.

2.4. Preparation of tablets

Powder mixtures, with FBP and THP content between 95 and 105%, were compacted using a manual hydraulic press equipped with 13.00 mm die set (Specac® Ltd, UK). The tablet weight was maintained at 300 ± 2 mg each and was compressed at 20 kN with a 30 s dwell time. All matrix tablets were stored in an airtight container over silica gel for 24 h before further investigation.

2.5. Swelling studies

Okra extract swelling studies were carried out for all formulations. Three bespoke metallic holders consisting of fine mesh of pore size 100 μm were weighed with a tablet (W_i) of each formulation, and placed into 10 mL of sodium phosphate buffer (pH 7.2) at 37.0 ± 0.5 °C. At 5, 15, 30, 60 and 120 min intervals, the previously weighed baskets containing the tablet were removed, lightly blotted with 125 mm filter paper (Whatman, UK) to remove excess water, reweighed (W_s) and were rapidly replaced into the glass vessels. The mean weight was determined for each formulation and degree of swelling (S) was calculated by using equation (1):

$$S = \frac{W_s - W_i}{W_i} \times 100 \quad (1)$$

where W_i and W_s are initial dry or swollen matrix tablet weight, respectively, at immersion time (t) in the buffer. The degree of swelling was determined from the mean of three replicates and presented as degree of swelling (S, %) against time (t).

2.6. Dissolution studies

The *in vitro* dissolution studies were performed on all okra extract-based hydrophilic matrices by using USP dissolution apparatus II, SR II 6-flask, basket apparatus (Hanson Research, USA). Phosphate buffer (900 ml at pH 7.2) was used as a dissolution medium and was maintained at 37.5 ± 0.5 °C. The paddle speed was adjusted to 75 rpm. Aliquots of dissolution medium (5 ml) were withdrawn manually after 5, 10, 15, 20, 25, 30, 60, 120, 240 and 360 min and replaced with an equal amount of fresh dissolution medium to maintain sink conditions. The dissolution samples were then analysed for drug content using UV–Vis spectrophotometry.

2.7. Preparation of emulsions

Oil-in-water emulsions with okra extracts at concentration 0.625% w/v with dispersed-phase (*n*-hexadecane) volume fraction $\varphi = 0.2$ and under acidic conditions (pH 3.0) were prepared as described previously (Alba et al., 2013). Briefly, the aqueous phases were magnetically stirred with hexadecane for 3 min in order to produce emulsion pre-mixes with oil volume fraction $\varphi = 0.2$ and 0.5% w/v final extract concentration in the entire emulsion. Processing conditions previously described (Alba et al., 2013) were used to fabricate emulsions with reproducible particle size distributions and investigate them during ageing. Consequently, the pre-

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