Saudi Pharmaceutical Journal xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Saudi Pharmaceutical Journal

journal homepage: www.sciencedirect.com

Original article

Cubic liquid crystalline nanoparticles containing a polysaccharide *from Ulva fasciata* with potent antihyperlipidaemic activity

Azza A. Matloub [a], Mona M. AbouSamra [b,*], Alaa H. Salama [b], Maha Z. Rizk [c], Hanan F. Aly [c], Ghada Ibrahim Fouad [c]

[a] Pharmacognosy Department, National Research Centre, Cairo, Egypt
[b] Pharmaceutical Technology Department, National Research Centre, Cairo, Egypt
[c] Therapeutic Chemistry Department, National Research Centre, Cairo, Egypt

ARTICLE INFO

Article history:
Received 31 October 2017
Accepted 5 December 2017
Available online xxxx

Keywords:
Ulva fasciata
Polysaccharide
Cubic liquid crystalline nanoparticle
Antihyperlipidaemic
Cubosomes

ABSTRACT

The present study involves the preparation of cubic liquid crystalline nanoparticles (cubsomes) for liver targeting to assess the potential of a formulated bioactive polysaccharide isolated from the hot aqueous extract of *Ulva fasciata* as an alternative natural agent with anti-hyperlipidaemic activity. Cubosomal nanoparticles were prepared by disrupting the cubic gel phase of the polysaccharide and water in the presence of a surfactant. Different lipid matrices and stabilizers were tested. All the formulations were in the nanosize range and showed sufficient negative charge to inhibit the aggregation of the cubosomes. Drug entrapment efficiencies (EEs%) were determined and in vitro release studies were performed. Transmission electron microscopy (TEM) and differential scanning calorimetry were used to analyze the loaded cubosomal nanoparticles containing glyceryl monostearate (GMO 2.25 g), poloxamer 407 (0.25 g) and 50 mg of the polysaccharide. A preclinical study comparing the cubic liquid crystalline nanoparticles containing polysaccharide to *fluvastatin* as a reference drug in hyperlipidaemic rats was conducted. The rats treated with the polysaccharide- loaded cubosomes showed significant decreases in total cholesterol (TC), triglycerides (TG) and total lipid (TL) compared to the untreated HL rats. In addition, oxidative stress and antioxidant biomarkers were measured in the HL rats. Compared to the untreated HL rats, the cubosome treated rats showed a significant reduction in malondialdehyde (MDA), whereas insignificant changes were detected in nitric oxide (NO), glutathione (GSH) levels and total antioxidant capacity (TAC). Further, vascular and intercellular adhesion molecules (VCAM, ICAM), and myeloperoxidase were demonstrated. A histopathological examination was conducted to study the alterations in histopathological lesions and to document the biochemical results. In conclusion, this study demonstrates the superiority of using a natural lipid regulator such as polysaccharide loaded cubosomes instead of *fluvastatin*.

© 2017 The Authors. Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

One of the most important goals in the pharmaceutical industry is targeting drugs to specific organs and tissues. In this context, the search for new drug delivery approaches and new modes of action represents one of the main challenges at present. The advances necessary to improve the therapeutic index and bioavailability of systems capable of site-specific delivery require a multidisciplinary scientific approach (Haag and Kratz, 2006; Korting and Schafer-Korting, 2010; Semete et al., 2010; Wang et al., 2011). With the increased usage of nanotechnology, nanomedicine has emerged as a strategy for the production of commercially available drug products. Nanomedicine involves the innovative use of nanometer scale materials to develop new approaches and therapies. Because of their characteristic small size, surface structure and high surface area, materials exhibit unique physicochemical properties (Semete et al., 2010). Such properties facilitate the intracellular uptake of nanomaterials to specific cellular targets, helping overcome the current limitations of traditional formulations.

* Corresponding author at: Pharmaceutical Technology Department, National Research Centre, 33 El-Buhouth Street, Dokki, Giza 12622, Egypt.
E-mail addresses: m_mona14@hotmail.com, mm.samra@nrc.sci.eg (M.M. AbouSamra).

Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

https://doi.org/10.1016/j.jsps.2017.12.007
1319-0164/© 2017 The Authors. Production and hosting by Elsevier B.V. on behalf of King Saud University.
This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Fatty liver disease is a reversible condition where large vacuoles of triglyceride fat accumulate in liver cells *via* the process of steatosis (i.e. abnormal retention of lipids within a cell). Fat accumulation may be accompanied by a progressive inflammation of the liver (hepatitis), i.e., steatohepatitis (Katiyar et al., 2016). In a previous study performed in our lab, we proved that a polysaccharide from *Ulva fasciata* polysaccharide was an effective anti-hyperlipidaemic agent (Matloub et al., 2013; Borai et al., 2015; Rizk et al., 2016a, 2016b). Polysaccharides a family of active materials similar to sialic acid; enhances the negative charges on cell surfaces to affect the aggregation of cholesterol in the blood, thereby, decreasing serum cholesterol levels (Li et al., 2008).

Cubic liquid crystals, also known as cubosomes, are dispersed nanostructured particles characterized by high biocompatibility and bioadhesive properties (Spicer, 2005). Cubosomes are produced in a liquid crystalline phase with cubic crystallographic symmetry and are formed by the self-assembly of amphiphilic or surfactant like molecules (Scriven, 1976). However, the cubic phases possess the unique property of very high solid like viscosity: because of their interesting bicontinuous structures, which enclose two distinct regions of water separated by a controlled bilayer of surfactant (Rizwan et al., 2007). Consequently, the cubic phases can be fractured and dispersed to form particulate dispersions that are colloidal and thermodynamically stable for a long time (Scriven, 1976). Cubosomes are characterized by their capability to encapsulate hydrophilic, hydrophobic and amphiphilic substances (Gustafsson et al., 1997; Bei et al., 2010). They also enable targeted and controlled drug release (Bei et al., 2010) and easily prepared and low cost.

This work describes a simple method for preparing a cubic phase gel matrix containing the polysaccharide isolated from the hot aqueous extract of *Ulva fasciata*. The prepared cubic gel matrix could be dispersed in water to form cubosomal nanoparticle dispersion prior to oral administration.

The polysaccharide-loaded cubosomes were evaluated for their *in vitro* and *in vivo* characteristics to explore their potential as a targeted drug delivery system providing optimal concentration of polysaccharide to the liver tissues.

2. Materials

The polysaccharide was isolated from the hot aqueous extract of *Ulva fasciata* as described by Matloub et al. (2013). Glyceryl mono-oleate (GMO), glyceryl mono-stearate (GMS), poloxamer 407 and poloxamer 188 were purchased from Sigma-Aldrich Chemical Company (Milwaukee, USA). Cellulose membrane dialysis tubing (molecular weight cut-off of 12,000–14,000 g/mole); was purchased from Sigma-Aldrich Chemical Company; St. Louis, USA. Fluvastatin was purchased from NOVARTIS Pharmaceuticals (Egypt, Cairo). Enzyme –linked immunoadsorption assay (ELISA) kits were provided by UCSN (U.S.A.) for myeloperoxidase (MPO) and Eiaab (USA) for both vascular cell adhesion molecule-1 (VCAM-1) and soluble intracellular adhesion molecule-1 (ICAM-1). Other chemicals and reagents were purchased from Biodiagnostic Company for Diagnostic and Research Reagents; (Egypt). All solvents and reagents were of analytical grades.

3. Methodology

3.1. Acquisition of the extract calibration curve using the sulfuric acid - UV method

The procedure for the proposed sulfuric Acid–UV method is as follows. A 1 ml aliquot of carbohydrate solution was rapidly mixed with 3 ml of concentrated sulfuric acid in a test tube and vortexed for 30 s. The temperature of the mixture increases rapidly within 10–15 s after the addition of sulfuric acid. Then, the solution was cooled on ice for 2 min to bring it to room temperature. Finally, the UV light absorption of the sample was read using a UV spectrophotometer (Shimadzu UV spectrophotometer 2410/PC, Japan) at 322 nm. Reference solutions were prepared according to the same procedure described above, except that the carbohydrate aliquot was replaced with distilled water (Albalasmeh et al., 2013).

3.2. Preparation of blank and drug- loaded cubic gels

For a blank cubic gel, GMO or GMS (2.25 g) and poloxamer 407 (0.25 g) or poloxamer 188 (0.25 g) were melted at 70 °C in a water bath. The obtained molten solution was added dropwise to 4 ml of deionized water (70 °C) and vortexed. The solution was mixed at high speed at room temperature to achieve a homogenous state. The mixture was equilibrated at room temperature for 48 h to obtain the blank cubic gel (Nasr et al., 2015). The drug-loaded cubic gel was prepared by dissolving 50 or 100 mg of extract in 4 ml of deionized water before adding the GMO or GMS/poloxamer 407 or poloxamer 188 molten solutions. The prepared formulations were subjected to physical examination to identify the homogenous gel and the separated system. The remaining steps were the same steps as those described for the preparation of the blank cubic gel. The cubic gels were stored at ambient temperature until use.

3.3. Preparation of cubosomal nanoparticles dispersions

To prepare the cubosomal dispersions, the cubic gel was dispersed in 18.50 ml of deionized water by vortexing at high speed for 3 min. The final concentration of lipids in the dispersion was 10% (*w*/*w*) with respect to the final dispersion weight. The final extract concentration in the cubosomal dispersion was 2 mg/g cubosomal dispersion.

3.4. Characterization of cubosomes

3.4.1. Particle size

The average diameter of the cubosomal dispersions and polydispersity index (PDI) were determined by photon correlation spectroscopy (PCS) using a Zetasizer Nano ZS (Malvern Instruments, Malvern, UK) at a fixed angle of 90° and at 25 °C. The aqueous cubosomal dispersions were diluted with distilled water before analysis. Each value represents the average of 3 measurements.

3.4.2. Zeta potential analysis

The particle charge was quantified as zeta potential (ZP) using a Zetasizer Nano ZS (Malvern Instruments, Malvern, UK) at 25 °C. Before measuring, each sample had to be diluted with demineralized particle free water to reach an adequate intensity. Each measurement was performed at least in triplicate.

3.5. Determination of drug entrapment efficiency and drug loading capacity

The entrapment efficiency (E.E.) was determined by measuring the concentration of drug in the supernatant after centrifugation using a cooling centrifuge (Union 32R, Korea). The unentrapped drug was determined by adding 1 ml of drug-loaded cubic gel to 9 ml of water and then centrifuging this dispersion at 9000 rpm and 4 °C for 30 min. The supernatant was collected, filtered through a Millipore membrane filter (0.2 μm), then diluted with water and measured using the sulfuric-acid-UV method against a blank. The E.E. was calculated using the following equation (Hou et al., 2003; Souto et al., 2004):

Please cite this article in press as: Matloub, A.A., et al. Cubic liquid crystalline nanoparticles containing a polysaccharide *from Ulva fasciata* with potent antihyperlipidaemic activity. Saudi Pharmaceutical Journal (2017), https://doi.org/10.1016/j.jsps.2017.12.007

Download English Version:

https://daneshyari.com/en/article/8522488

Download Persian Version:

https://daneshyari.com/article/8522488

Daneshyari.com