ASIAN JOURNAL OF PHARMACEUTICAL SCIENCES 10 (2015) 425–432

HOSTED BY

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/ajps

Original Research Paper

Solid lipid microparticles: An approach for improving oral bioavailability of aspirin

T.H. Gugu [a], S.A. Chime [a,*], A.A. Attama [b]

[a] Department of Pharmaceutical Technology and Industrial Pharmacy, University of Nigeria, Nsukka 410001, Nigeria
[b] Department of Pharmaceutics, University of Nigeria, Nsukka 410001, Nigeria

ARTICLE INFO

Article history:
Received 14 February 2015
Received in revised form 13 June 2015
Accepted 24 June 2015
Available online 14 July 2015

Keywords:
Solid lipid microparticles
Ulcer inhibition
NSAIDs
Anti-inflammation
Lipids

ABSTRACT

The objectives of the work were to develop a lipid based delivery system for aspirin and to evaluate its physicochemical and pharmacodynamic properties. Aspirin-loaded solid lipid microparticles (SLMs) were formulated by hot homogenization and analysed for their encapsulation efficiency (EE%), *in vitro* release, particle size, anti-inflammatory and ulcer inhibition properties. Particle size ranged from 33.10 ± 5.85 to 43.50 ± 7.27 μm for batches A1 to A3 SLMs loaded with 1, 3 and 5% aspirin and containing Poloxamer 407, while batches B1, B2 and B3 formulated with Soluplus as surfactant had particle size range of 31.10 ± 1.46 to 45.60 ± 2.92 μm. Batches A1 and B1 containing 1% of aspirin had the highest EE of 70 and 72% respectively. Maximum *in vitro* release of 95.1 and 93.2% were obtained at 8 h from batches A1 and B1 respectively. SLMs exhibited about 77.8% oedema inhibition, while the reference had 66.7% and ulcer inhibition range of 25–75%. Aspirin-loaded SLMs exhibited good properties and could be used orally twice daily for the treatment of inflammation.

1. Introduction

Aspirin is one of the oldest drugs used in the treatment of pain and inflammation; however, recently this drug has been prescribed for a host of indications. In addition to its use as an analgesic, anti-inflammatory, and antipyretic agent, it is indicated for use in the prevention and treatment of heart disease and stroke [1]. Further studies are under way investigating the potentials of aspirin in boosting the immune system, treating cognitive decline, and lowering the risk of colon and ovarian cancer [1]. Despite these attributes, it suffers a lot of side effects with the gastrointestinal (GI) side effect being the most prominent in patients on daily dose of aspirin. Aspirin has been regarded as a potential gastric irritant and studies have shown that the incidence of gastrointestinal side effects may in-

* *Corresponding author.* Department of Pharmaceutics, University of Nigeria, Nsukka 410001, Nigeria. Tel.: +234 8061329790; fax: +234 42 771709.
E-mail addresses: salome.chime@unn.edu.ng; emmymarachi@yahoo.com (S.A. Chime).
Peer review under responsibility of Shenyang Pharmaceutical University.
http://dx.doi.org/10.1016/j.ajps.2015.06.004

crease with regular use [1]. Because of this, aspirin is preferably formulated in the form of enteric coated formulations.

Aspirin is a moisture-sensitive drug and can hydrolyse into acetic and salicylic acids when exposed to high humidity and elevated temperatures, coating could subject aspirin tablets to both high temperatures and humidity [1]. Mitrevej and Hollenbeck found that a hydrophilic field generated around aspirin crystals under high-humidity conditions and upon combining the drug with certain tablet excipients like hydrophilic disintegrants may lead to condensation of aspirin crystals [2]. Because of all these problems encountered in formulating aspirin tablets, the GI side effects and because of the importance of this drug in the treatment of ailments, a new delivery system that will prevent the GI side effects as well as reduce the rigors involved in formulation is very important so as to enhance patient acceptability of this drug, reduce or eliminate gastric irritation and enhance the efficacy of this drug [1].

Solid lipid microparticles (SLM) are micro-scale drug carriers possessing a matrix made from fatty acid, glyceride, fatty alcohol, and solid wax with high melting points [3]. They combine many advantages of drug carrier systems. The amount of drug encapsulated can vary up to 95% for lipophilic and hydrophilic drugs and because they are made from physiological or physiologically related materials, they are well tolerated in living systems. The solid matrix protects loaded labile substances against degradation and it offers the possibility of controlled drug release and drug targeting [4–6]. Compared to the polymer microparticles, SLMs have the advantage of better biocompatibility, which minimizes the hazards of acute and chronic toxicity; they possess solid cores which reduce the mobility of incorporated drug and drug leakage from the carriers. They can be produced on a large industrial scale and are easy to produce [7,8]. They also have the ability to mask the taste of some drugs and have been shown to enhance the absorption of both hydrophilic and lipophilic drugs and have been shown to protect the GI against the gastric irritation side effects of non steroidal anti-inflammatory drugs (NSAIDs) [5–9]. Because of all these quality attributes of SLMs, we decided to investigate its properties on aspirin. Therefore, the aims of the work were to formulate aspirin-loaded SLMs in order to investigate its ability to protect the drug from hydrolysis, and also to study the anti-inflammatory and anti ulcer properties of the formulations.

2. Materials and methods

2.1. Materials

The following materials were used as supplied by the local suppliers with no further modifications: Phospholipon® 90H (Phospholipid GmbH, Köln, Germany), sorbic acid (Sigma® Chemical Company, USA), sorbitol (Qualikems Laboratory Reagent, India), Poloxamer® 407 (Synochem City, Germany), Soluplus®, sodium hydroxide, monobasic sodium phosphate (Merck, Darmstadt, Germany), goat fat (Quarter market, Awka, Nigeria), activated charcoal (Bio–Lab, UK), aspirin (Evans Pharmaceutical Ltd., England), and distilled water (Lion Water, Nsukka, Nigeria).

2.2. Extraction of goat fat

The fat was extracted by grating the adipose tissue prior to boiling with half its weight of water on a water bath for 45 min. Molten fat was separated from the aqueous phase using a muslin cloth. Further purification was carried out by heating a 2% w/w suspension of a 1:9 ratio blend with activated charcoal and bentonite at 80–90 °C for 1 h. Thereafter, the suspension was vacuum-filtered using Buchner funnel [10].

2.3. Preparation of lipid matrix (LM)

The lipid matrix was prepared by fusion using Phospholipon® 90H (30 g) and purified goat fat (70 g). The lipids were weighed and melted together in a beaker placed on a magnetic stirrer hot plate (SR1 UM 52188, Remi Equip., India) at 70 °C and stirred with a glass stirrer until a transparent homogenous white melt was obtained. The lipid matrix was stirred continuously until it solidified at room temperature [6].

2.4. Formulation of the SLMs

The aspirin-loaded SLMs were prepared using the melt homogenization technique according to the formula presented in Table 1. In each case, 5 g of the lipid matrix was melted at 80 °C on a water bath and an appropriate amount of aspirin was incorporated into the lipidic melt. Sorbitol, Soluplus or poloxamer as the case may be were dissolved in hot distilled water at the same temperature with the lipidic melt. The hot

Table 1 – Formula for different batches of SLMs.

Batch	LM (%)	Aspirin (%)	Soluplus® (%)	Poloxamer 407 (%)	Sorbitol (%)	Sorbic acid (%)	Distilled water (%)
A1	5	1	–	4	4	0.05	100
A2	5	3	–	4	4	0.05	100
A3	5	5	–	4	4	0.05	100
A4	5	–	–	4	4	0.05	100
B1	5	1	2	–	4	0.05	100
B2	5	3	2	–	4	0.05	100
B3	5	5	2	–	4	0.05	100
B4	5	–	2	–	4	0.05	100

A1, A2, A3 and A4 were formulated with Poloxamer 407 and contain 1, 3, 5 and 0% aspirin respectively, while, B1, B2, B3 and B4 were formulated with Soluplus and contain 1, 3, 5 and 0% aspirin respectively.