Journal of Applied Pharmaceutical Science Vol. 3 (10), pp. 008-010, October, 2013
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2013.31002
ISSN 2231-3354 

Prolonged-release lipid microparticles prepared with decyl oleate and hydrogenated castor oil of ibuprofen

Felipe Cardoso Rodrigues Vieira[1], Maria Helena dos Anjos Rodrigues Amaral[2] and Paulo Alexandre Lourenço Lobão[2]
[1]Faculty of Pharmacy, University Federal of Piaui, Teresina, Brazil.
[2]Pharmaceutical Technology Service, Faculty of Pharmacy, University of Porto, Porto, Portugal.

ARTICLE INFO

Article history:
Received on: 10/09/2013
Accepted on: 29/09/2013
Available online: 31/10/2013

Key words:
Ibuprofen, Lipid microparticles, Decyl oleate, Hydrogenated castor oil.

ABSTRACT

Ibuprofen is one of the most important non-steroidal anti-inflammatory drugs used in the treatment of inflammatory diseases. In its pure state, ibuprofen presents poor physical and mechanical characteristics and its use in solid dosage forms needs the addition of excipients that improve these properties. The selection of the best excipients and the most suitable pharmaceutical dosage form to carry ibuprofen is very important for the industrial success of this drug. Given these factors, lipid microparticles of ibuprofen with decyl oleate and hydrogenated castor oil were prepared. This formulation was intended to improve the content of ibuprofen in preparation and to sustain the release of this drug. Lipid microparticles were submitted to determination of ibuprofen content using UV-VIS spectrophotometry and, gelatin capsules filled with lipid microparticles and tablets prepared with these microparticles were submitted to dissolution tests in order to study the influence of the prepared system in the release profiles of ibuprofen. The improvement of the content of ibuprofen and prolonged release of this drug was achieved with the lipid microparticles prepared with this mixture of excipients.

INTRODUCTION

Ibuprofen (IB) is a drug of the non-steroidal anti-inflammatory group (NSAIDs), belonging to the subgroup of drugs derived from propionic acid (Oswald, 2001). It is generally well tolerated, but may trigger headaches, stomach pain, vomiting, diarrhea, stomach and duodenal ulcers (Brunton *et al.*, 2007). Therefore, there is a need to minimize these adverse effects and to prolong its anti-inflammatory action. There are two key strategies to alter the release and subsequent absorption of drugs, one is based on its modification and the other is based on the modification of the dosage form (Lachman, 2001). Microparticles arise from the need to overcome possible adverse effects and to increase the short half-life of some drugs. The main advantages are the fact that they present a great biocompatibility, low toxicity, high stability, and improve efficacy, absorption, and bioavailability. They can also facilitate the administration, masking the organoleptic properties and protecting the drug (Kumar, 2000).

* *Corresponding Author*
Felipe Cardoso Rodrigues Vieira, Faculty of Pharmacy, University Federal of Piaui, Teresina, Brazil, Ministro Petrônio Portella University Campus, Ininga District, 64049–550 – Teresina, Brazil.
Phone: +55 8698432932

The microparticles have dimensions that can vary between 1 μm and 1000 μm; however, some authors have considered particles larger than 1 mm as microparticles. The microparticles can be classified as reservoirs or matrices. In the first case, the drug is at the core and is surrounded by a layer or film coating, which can be semi-permeable or completely permeable. In the second case, the drug is homogeneously dispersed in a matrix of irregular geometry and that is sometimes porous. The drug can be found on the surface of the matrix in direct contact with the external environment. There are several methodologies for the production of microparticles reflecting the physicochemical properties of the drug in order to maintain their unique therapeutic properties. However, there are other factors to take into account such as: the environmental impact of the process; ease of implementation; availability of equipment and resources; cost; and process efficiency. The methods for the production of lipid microparticles include: spray-drying technology (Mahajan, 2009); double-emulsion solvent evaporation (Freitas *et al.*, 2005); emulsion/ chilling, the solvent method (Soppimath, 2001); the engineering division, fluid supercritical (Kang *et al.*, 2008); atomization and modified atomization; fluidized bed (Gouin, 2004); and extrusion. The choice of a matrix for incorporation of the drug is very important, because this choice will influence the ability of the

formulation to control the drug release and thereby sustain the therapeutic action over time (Salomen, 1980). Waxes and other related lipidic materials such as hydrogenated castor oil, form matrices that control the release of drugs by diffusion through pores or by erosion. Decyl oleate is used in the pharmaceutical industry as a softening agent and in preparation of emulsions (Rowe *et al., 2003*).

MATERIALS AND METHODS

Materials

Ibuprofen (Lot No. 082374, Acofarma, Spain), hydrogenated castor oil (Cutina HR®) (Lot No. CG42720170, José M. Vaz Pereira SA, Portugal), decyl oleate (Cetiol-V®) (Lot No. 072069, Acofarma, Spain), monosodium phosphate (Lot No. 0194, José M. Vaz Pereira, SA, Portugal), disodium phosphate anhydrous (Lot No. 130470JR, José M. Vaz Pereira, SA, Portugal), propylene glycol (Lot No. VF251920D4, José M. Vaz Pereira, SA, Portugal), polysorbate 80 (Tween® 80) (Lote n.º 609D0241, José M. Vaz Pereira, SA, Portugal), chloroform (Lot No. 7B128128C, Pronolab, José M. Vaz Pereira, SA, Portugal) and gelatin capsules No. 0 (Lot No. 9328900023, Guinama, Spain).

Methods

Preparation of lipid microparticles containing ibuprofen

Lipid microparticles of 1:2 ibuprofen/excipient ratio (where, 1:3 decyl oleate/hydrogenated castor oil ratio composed the excipient) were prepared using the emulsion/chilling method. Excipients were melted (variable temperature according to the melting point of the excipients) on a hot plate under stirring at 600 rpm (in order to achieve particles with micrometric size) and ibuprofen was added to the molten excipient. The oil phase was slowly added to a 1.5 % (w/w) Tween® 80 solution at the same temperature, followed by the quick addition of a mixture of water : propylene glycol (75:25) at 0 °C, maintaining the agitation at 600 rpm. The microparticles obtained were filtered and washed with water. Gelatin capsules No. 0 were filled with these lipid microparticles (method - capsule filling plate). Tablets were prepared with the aid of a hydraulic manual and a force of 0.5 tons. The theoretical average weight was 300 mg.

Determination of ibuprofen content using UV-VIS spectrophotometry

For the determination of ibuprofen content in lipid microparticles, 75 mg of sample was dissolved in chloroform (50 mL) and analyzed by UV-VIS spectrophotometry (UV-VIS spectrophotometer JASCO V-650, Japan) at 272 nm. The accuracy, repeatability, specificity, and linearity of the spectrophotometric method were previously evaluated.

In vitro dissolution test

For this study, gelatin capsules containing lipid microparticles, capsules containing only pure Ibuprofen and tablets prepared with lipid microparticles were used. Dissolution tests were performed under the following conditions:

- Dissolution apparatus - SOTAX AT7 (Switzerland);
- Basket method;
- Agitation speed - 100 rpm;
- Temperature – 37.0 ± 0.5 ºC;
- Dissolution liquid - pH 7.4 phosphate buffer solution (Portuguese Pharmacopoeia IX);
- Dissolution liquid volume - 500 mL;
- Sample bulk - 10.0 mL;
- Collection times - 30, 60, 120, 240, 360, 600 minutes.

Samples were assayed in triplicate in a UV-VIS spectrophotometer at 272 nm, using pH 7.4 buffer phosphate solution as a blank.

RESULTS AND DISCUSSION

Determination of ibuprofen using UV-VIS spectrophotometry

For ibuprofen UV-VIS spectrophotometry determination, several validation parameters were evaluated. The method showed specificity, good linearity (coefficient of determination of 0.999), accuracy (101.30% ± 2.55), and repeatability (CV = 0.34%) within the range of concentrations assayed. Table I presents the ibuprofen content in the lipid microparticles prepared with decyl oleate and hydrogenated castor oil.

Table. 1: Ibuprofen content in lipid microparticles.

Lipid microparticles	% of ibuprofen
LM 1:3 DO/HCO	69.50

(LM 1:3 DO/HCO - lipid microparticles of decyl oleate and hydrogenated castor oil).

The results of the determination of ibuprofen content in lipid microparticles prepared with decyl oleate and hydrogenated castor oil showed a percentage of ibuprofen of 69.50%. Thus, is slightly higher percentage of ibuprofen in these microparticles than those prepared with only the hydrogenated castor oil (67.56%) as reported by Andrade, 2012; what can be due the emulsifying properties of decyl oleate which confers to preparation higher encapsulation of drug.

In vitro dissolution test

After the preparation and characterization of capsules and preparation of tablets, *in vitro* dissolution studies were performed. Validation parameters of the method for ibuprofen determination (UV-VIS spectrophotometry) were evaluated. The method showed specificity, good linearity (coefficient of determination of 0.9994), accuracy (100.43% ± 1.97), and repeatability (CV = 0.18%) within the range of concentrations studied.

As can be seen in Figure 1, about 95% of pure ibuprofen was dissolved in the first 30 minutes of the dissolution test. The lipid microparticles of decyl oleate and hydrogenated castor oil in gelatin capsules showed a higher percentage of ibuprofen released (48.65%) after 30 minutes of in vitro dissolution test. After 10 hours of testing, the amount of ibuprofen released from the lipid microparticles of decyl oleate and hydrogenated castor oil was

60.30%. Thus, is slightly higher percentage of ibuprofen was dissolved in the test with these microparticles than those prepared only with the hydrogenated castor oil (59.60%) as reported by Andrade, 2012.

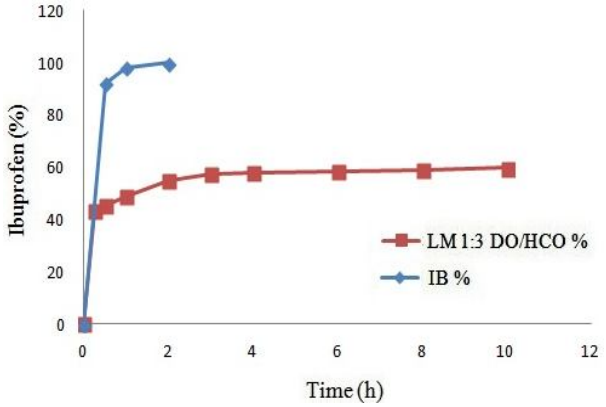

Fig. 1: Dissolution profile of pure ibuprofen and lipid microparticles of decyl oleate and hydrogenated castor oil in gelatin capsules (LM 1:3 DO/HCO % – percentage of ibuprofen in lipid microparticles of decyl oleate and hydrogenated castor oil).

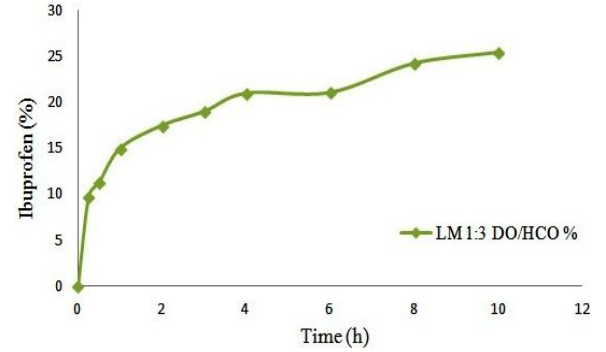

Fig. 2: Dissolution profile of tablets prepared with lipid microparticles of decyl oleate and hydrogenated castor oil (LM 1:3 DO/HCO % - percentage of ibuprofen in lipid microparticles of decyl oleate/hydrogenated castor oil).

Figure 2 show that, the tablets prepared with lipid microparticles of decyl oleate and hydrogenated castor oil showed a little percentage of ibuprofen released (11.27%) after 30 minutes of in vitro dissolution test. After 10 hours of testing, the amount of ibuprofen released from tablets was 25.44%.

The presence of lipids appears to affect the crystalline organization of ibuprofen. Solid lipid microparticles were highly in amorphous form, in contrast to pure ibuprofen, which contributed to a decrease of dissolution/release of this drug. Besides, the sustained release profiles of solid dispersions and lipid microparticles can be attributed to the entrapment of drug in the lipid matrices. The dissolution/release of ibuprofen is more sustained and retarded in tablets prepared with the lipid microparticles than in gelatin capsules due to their own pharmacokinetic properties of that pharmaceutical form.

CONCLUSIONS

The results of this work showed that type of excipients have influence in ibuprofen content in the lipid microparticles prepared, as well as, in the dissolution profiles of this drug. The lipid microparticles prepared with decyl oleate and hydrogenated castor oil showed an ibuprofen content higher than preparations with only hydrogenated castor oil and a sustained-release of this drug. Prolonged-release of ibuprofen was achieved both in tablets prepared with lipid microparticles as in gelatin capsules, what does both of pharmaceutical forms important for carry of ibruprofen.

ACKNOWLEDGEMENT

The authors acknowledge financial support from CNPq (Brazilian National Council for Scientific and Technological Development) and structural support from Faculty of Pharmacy, University of Porto, Portugal.

REFERENCES

Almeida H, Amaral MH, Lobão P. Comparative study of sustained release lipid microparticles and solid dispersions containing ibuprofen. *Braz. J. Pharm. Sci*. 2012; 48(3): 529-536.

Brunton LL, Lazo JS, and Parker KL. 2007. Goodman & Gilman`s - as Bases Farmacológicas da Terapêutica. Rio de Janeiro, RJ: McGraw-Hill.

Freitas S, Merkle HP, Gander, B. Microencapsulation by solvent extraction/evaporation: reviewing the state of the art of microsphere preparation process technology. *J. Control. Release.* 2005; 102(2): 313-332.

Gouin S. Microencapsulation: industrial appraisal of existing technologies and trends. *Trends Food Sci. Technol.* 2004; 15(7-8): 330-347.

Kang Y, Yin G, Ouyang P, Huang Z, Yao Y, Liao X, Chen A, Pu X. Preparation of PLLA/PLGA microparticles using solution enhanced dispersion by supercritical fluids (SEDS). *J. Colloid Interface Sci*. 2008; 322(1): 87-94.

Kumar, MNV. Nano and microparticles as controlled drug delivery devices. *J. Pharm. Sci.* 2000; 3(2): 234-258.

Lachman L. 2001. Teoria e prática na indústria farmacêutica. Lisboa: Fundação Calouste Gulbenkian.

Mahajan HS, Gattani SG. Gellan gum based microparticles of metoclopromide hydrochloride for intranasal delevery: development and evaluation. *Chem. Pharm. Bull.* 2009; 57(4): 388-392.

Osswald W. 2001. Terapêutica medicamentosa e suas bases farmacológicas. Manual de Farmacologia e Farmacoterapia. Porto: Porto Editora.

Rowe RC, Sheskey PJ, Weller PJ. 2003. *Handbook of pharmaceutical excipients.* 4th ed. The Pharmaceutical Press, American Pharmaceutical Association, Washington. 776.

Salomen JL, Doelker E. Formulation of sustained release tablets. I. Inert matrices. Pharm. Acta Helv. 1980; 55(7): 174-182.

Soppimath KS, Kulkarni AR, Aminabhavi TM. Encapsulation of antihypertensive drugs in cellulose matrix microspheres: characterization and release of microspheres and tableted microspheres. *J. Microencapsul*. 2001; 18(3): 397-409.

How to cite this article:

Felipe Cardoso Rodrigues Vieira, Maria Helena dos Anjos Rodrigues Amaral and Paulo Alexandre Lourenço Lobão. Prolonged-release lipid microparticles prepared with decyl oleate and hydrogenated castor oil of ibuprofen. J App Pharm Sci, 2013; 3 (10): 008-010.