Journal of Applied Pharmaceutical Science 01 (06); 2011: 194-196

Journal of Applied Pharmaceutical Science

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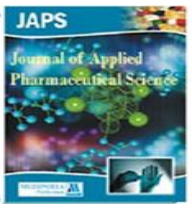

ISSN: 2231-3354
Received: 01-08-2011
Revised on: 05-08-2011
Accepted: 12-08-2011

Formulation of escitalopram emulsion using a novel bio- emusifier from unriped fruit pulp of *Artocarpus heterophyllus*

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ABSTRACT

The aim of our research work was to isolate a novel bio-material from unripe fruit pulp of *Artocaropus heterophyllus,* and to evaluate its bio-emulsifying ability by formulating escitalopram emulsions. The bio-material was isolated from the unripe fruit pulp of *Artocarpus heterophyllus* by simplified economic process. It was subjected for various physicochemical parameters like color, colour changing point, chemical tests, IR spectral study. Four Drug loaded emulsions were formulated(AH1-AH4) using varying ratios of the bio-material. The emulsions were formulated using Escitalopram as a model drug. The formulated emulsions were subjected for evaluation parameters like globule size, pH, effect of centrifugation, viscosity, surface tension, creaming, freezing and thawing cycles and *in-vitro* release. The infra red spectra of the bio-material showed the presence of saturated hydrocarbons, aromatic ring and secondary and tertiary alcohol groups. The emulsions showed a globule size in the range 0.15-0.17µm, viscosity of 11.4±0.5cp to 17.6±1.2cp, surface tension in the range 59.67±1.3 to 65.42±1.45 dyne/cm. The emulsions had content uniformity of 73%±2.1% to 81%±1.85%. The *in-vitro* drug release studies from the formulated emulsions exhibited a controlled release for a period of 8 hours. The formulation AH3 was found to be best formulation on the basis of evaluation parameters, *in-vitro* release study and stability study. It showed content uniformity of 77% and was found to be stable with no signs of phase separation, creaming and showed controlled release of more than 8 hours with t80% of more than 5.5 hours. The emulsions followed zero order release as shown by the higuchi model. The release curves were fitted to korsenmeyer equation and showed linear release profile.

Key words: *Artocaropus heterophyllus,* Escitalopram, emulsions, bio-material

INTRODUCTION

Emulsion formulation requires tedious study in order to check the most important parameters to obtain stable emulsions. Optimizing a process implies determination of the experimental conditions giving optimal performance. the optimal operating conditions will be applied emulsifiers, corresponding to the determination of the critical hydrophilic-lipophilic balance (critical HLB) of the emulsion. The dilemma in formulation of an emulsion lies in the fact that the success of such unstable systems can be judged only after a long time. Usually, when stability problems occur, formulation tests may be extended for a very long period. Accelerated testing could be applied to avoid this problem. Many methods are in use to evaluate destabilization processes, Emulsion stability is estimated by the average size of the droplets and the variation of emulsion viscosity. The smaller the emulsion droplet size and the smaller the viscosity variations, the better the stability of the system. The bio-polymers can be used to replace the existing synthetic polymers used for the preparation of pharmaceutical dosage forms.

The synthetic polymers that are used widely in pharmaceutical field are the cellulose derivatives like sodium carboxy methyl cellulose, HPMC, HPC, acrylic acid derived polymers, sodium alginate, pectin, acacia etc. these polymers being synthetic may precipitate adverse reactions in humans.

Jackfruit (*Artocaropus Heterophyllus)* belongs to the family moraceae, it contains morin, carotenoids, provitamin A. It is used medicinally as a laxative, tonic and demulcent. The drug atorvastatin is an HMG-Coenzyme inhibitor and is used for the treatment of hyperlipidimea i.e. elevated cholesterol levels in the body. It is generally administered once daily, the aim of our experiment is to formulate a ovel bio-polymeric based sustained release tablet of atorvastatin for once daily dosing. Jackfruit pulp contains morin and a crystalline constituent, cyanomaclurin, probably isomeric with catechins. It is a Good source of provitamin A carotenoids. It is also composed of a new flavonone, a new prenylfalvone, a novel phenolic compound, heterophylol and nine known flavonoids. Ripe fruit is used as demulcent, nutritive, laxative. Pulp or flesh surrounding the seed is aromatic, cooling and tonic. Also used in Diarrhea, fever and asthma.

Escitalopram (trade names Lexapro, Cipralex, Seroplex, Lexamil, Lexam) is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class. It is approved by the U.S. Food and Drug Administration (FDA) for the treatment of adults with major depressive disorder and generalized anxiety disorder (Cipriani et al, 2009).

In the current research a novel bio-material from the unripened fruit pulp of *Artocarpus heterophyllus* as a bio-emulsifier for the formlation of escitalopramm loaded emulsions.

MATERIALS AND METHODS

The drug escitalopram was obtained as a gift sample from Macleods Laboratories, Mumbai, India. Jackfruit was procured from the local market. All other reagents used were of highest purity and analytical grade. Double distilled water was used throughout the experimental work.

Bio-material extraction

The bio-material was isolated from the fruits of artocarpus heetrophyllus as per our previously published method. The bio-material was isolated from the unripe fruit pulp of *Artocarpus heterophyllus* by a simplified economic process (Madhav and Tangri, 2011).

Formulation of emulsions

The o /w emulsions were prepared by taking the specified amount of Escitalopram, bio-material and mixed with castor oil to form a homogenous system. Double distilled water was added dropwise to the oil phase to form the emulsion. The volume was made up by adding excess of water. Similar procedure was followed for other formulations. The emulsions were prepared in four ratios(AH1-AH4) by varying the amount of bio-material(20mg-100mg). The formulated emulsions were evaluated for the various evaluation parameters. (Table no. 1)

Table 1 Formulations Prepared.

Ingredients	AH1	AH2	AH3	AH4
escitalopram(mg)	10	10	10	10
castor Oil(ml)	5	5	5	5
Distilled Water (Ml)	2.5	2.5	2.5	2.5
Bio-material (mg)	20	40	80	100

Evaluation of emulsions

The emulsions were evaluated for globule size, in-vitro release study, viscosity, surface tension, content uniformity, stability studies. (table no. 2).

Table 2 Evaluation Parameters.

S.No.	Parameter	AH1	AH2	AH3	AH4
1.	Globule Size(µm)	0.153±0.034	0.161±0.046	0.159±0.052	0.175±0.032
2.	pH	6.2±0.2	6.3±0.1	6.1±0.25	6.2±0.3
3.	Surface tension	59.67±1.3	62.34±1.45	63.91±1.21	65.42±1.27
4.	Content uniformity	73±2.1	74±1.95	77±1.46	81±1.85
5.	Viscosity(Cps)	11.4±0.5	13.9±1.3	17.6±0.84	16.3±1.5
6.	Freze and thaw cycle	6±1	6±1	6±1	7±1

Globule size determination

The diameter of the droplets was measured with an optical microscope equipped with a calibrated eyepiece micrometer. The mean diameter was calculated on the basis of at least 100 droplets. Mean of three readings was reported. All measurements were taken after 24 h.(Carlotti et al, 1993)(table no.2, fig no.1).

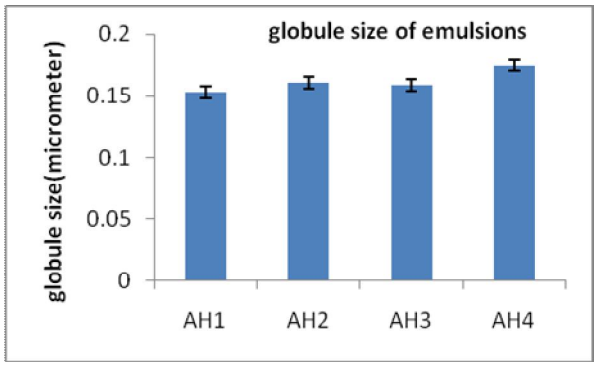

Fig. 1 Globule size of emulsions

pH value

pH value of freshly prepared emulsions and emulsions kept at different conditions were determined by a digital pH-Meter. The study was replicated for three readings.(Carlotti, 1993)(table no.2).

Rheological study

Viscosity measurements were made by using Brookfield viscometer, at constant temperature (25°C) at 100 rev/ min. Readings performed in triplicate (Kato et al, 1968)(table no.2, fig. no. 2).

Centrifuge tests

Centrifugal tests were performed for emulsions immediately after preparation. The centrifugal tests were repeated for the emulsions after 24 hours, 3 days, 7 days, 14 days and 28 days of preparation (Latreille and Paquin, 1990).

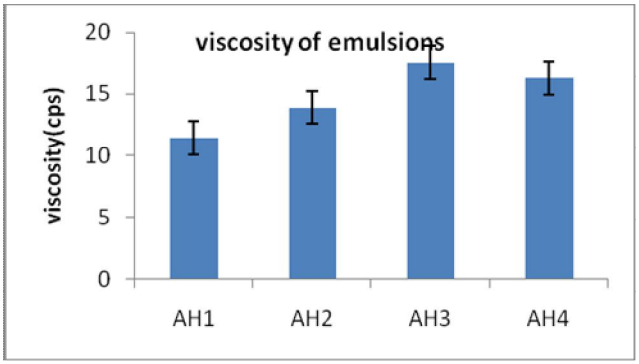

Fig. 2 Viscosity of emulsion.

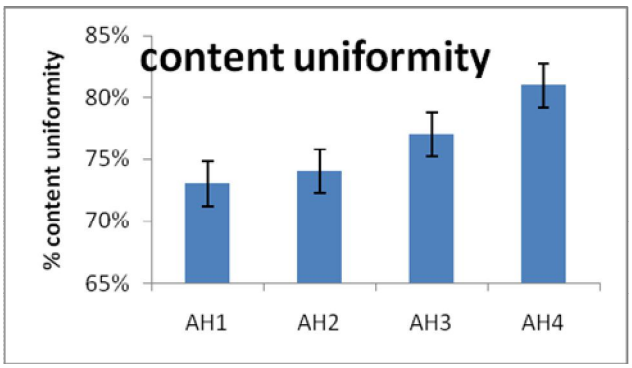

Fig. 3 Content uniformity of emulsions.

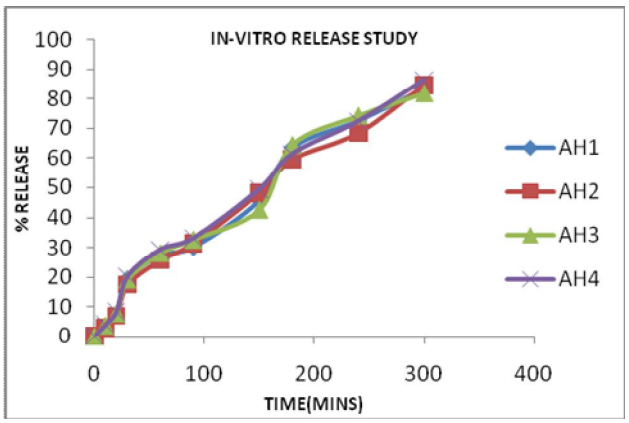

Fig. 4 *In-vitro* release study of emulsions.

Stability tests

Stability tests were performed at different storage conditions for both primary and multiple emulsions to see the effect of these conditions on the storage of both primary and multiple emulsions. These tests were performed on samples kept at 8˚C ± 0.1˚C (in refrigerator), 25˚C ± 0.1˚C (in oven), 40˚C ± 0.1˚C (in oven) and 40˚C ± 0.1˚C (in oven) with 75% relative humidity (RH). Organoleptic characteristic of both primary and multiple emulsions, i.e. color, liquefaction and phase separation were noted at various intervals for 28 days (Latreille and Paquin, 1990).

RESULTS AND DISCUSSIONS:

A novel bio-polymer from *Artocarpus heterophyllus* was isolated by simplified economical process the yield was 1%. The bio-polymer obtained was of brownish to dark brown colour with a colour changing point of 160-165˚. The bio-polymer showed positive tests for the presence of proteins and carbohydrates. The infra red spectra of the bio-material showed the presence of saturated hydrocarbons(2925.81 cm^{-1}), aromatic ring(1598.18 cm^{-1}) along with secondary and tertiary alcohol groups(1078.13 cm^{-1}, 1151.42 cm^{-1}). The emulsions showed a globule size in the range 0.15-0.17µm, viscosity of 11.4±0.5cp to 17.6±1.2cp, surface tension in the range 59.67±1.3 to 65.42±1.45 dyne/cm. The emulsions had content uniformity of 73%±2.1% to 81%±1.85%. The *in-vitro* drug release studies from the formulated emulsions exhibited a controlled release for a period of 8 hours. The formulation AH3 was found to be best formulation on the basis of evaluation parameters, *in-vitro* release study and stability study. It was found to be stable with no signs of phase separation, creaming and showed controlled release of more than 8 hours with t80% of more than 5.5 hours. The emulsions followed zero order release as shown by the higuchi model. The release curves were fitted to korsenmeyer equation and showed linear release profile. The formulations were found to be stable after a period of 28 days at various conditions of temperature and humidity.

CONCLUSION

The research work gives an insight to the use of potential bio-materials for the formulation of various dosage forms. It shows the potential bio-emulsifying ability of bio-material from *Artocarpus heterophyllus*. Finally the conclusion was drawn that the isolated bio-material can serve as a novel bio-emulsifier for formulating various drug loaded emulsions.

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