International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol. 3, No.2, pp 929-933, April-June 2011

A Novel, Potent, Bio-Emulsifier From the Fruit Pulp of *Manilkara zapota* for formulating Escitalopram Microemulsions

N.V. Satheesh Madhav[1]*, Shaffi Khurana[1]

[1]Dehradun Institute of Technology- Faculty of Pharmacy, Mussoorie Diversion Road, village Makkawala, P.O. Bhagwantpura-248009, Dehradun, Uttarakhand, India.

Corres.author: satheesh_madhav@yahoo.com, shaffi.khurana@yahoo.in
Tel.: 091 9760203573, 091 9927760066

Abstract: *Manilkara zapota* fruit pulp consists of sapotin, saponin ,fixed oils and bitter alkaloids. The current aim of our research work is to isolate a novel bio-material from the fruit pulp of *manilkara zapota* and to evaluate its bio-stabilizing ability by formulating various escitalopram emulsions using almond oil as oil phase and bio-material as bio stabilizer. The bio-material was isolated from the fruit pulp of *manilkara zapota* by simplified economical method. Three different escitalopram emulsions was formulated using bio stabilizer in different concentrations. The formulated emulsions were subjected for various evaluation parameters like globule size, ph, effect of centrifugation, viscosity, surface tension and rate of drug release. The formulated emulsions exhibit uniform globule size, promising stability against centrifugation effect in comparison to standard emulsion. The drug release studies from the formulated emulsions exhibited a promising stability, transparency, uniform globule size range, surface tension and sustainability for a period of 8 hours. Finally the conclusion was drawn that the isolated bio stabilizer acts as novel emulsifier for formulating various drug loaded micro emulsions.
Key words: microemulsions, Escitalopram, *manilkara*, emulsifier.

Introduction and Experimental:

The current aim of our research work is to isolate a novel bio-material from the fruit pulp of *manilkara zapota* and to evaluate its bio-stabilizing ability by formulating various escitalopram emulsions using almond oil as oil phase and bio-material as bio stabilizer. The bio-material was isolated from the fruit pulp of *manilkara zapota* by simplified economical method.

Manilkara zapota(sapodilla) consists of sapotin, saponin, achrassaponin, an alkaloid, fixed oil. It is used in the treatment of kidney stones, fever and rheumatism.escitalopram is an antidepressant drug. The antidepressant effect of escitalopram is presumed to be linked to specific serotonin (5-hydroxytryptamine [5-ht]) reuptake inhibition.

Micro emulsion is defined as monophasic[1], thermodynamically stable, transparent(sometimes translucent),isotropic, liquid mixture.it is a colloidal dispersion of oil and water which is stabilized by interfacial surface film of low viscosity[2,3].the interfacial tension in micro emulsion is reduced by use of surfactant in combination with a co-surfactant[4].the globule size of a micro emulsion lies between 10-100 nm[5,6].micro emulsion acts as a drug carrier for percutaneous, ocular, oral and parenteral administration[7].the use of micro emulsion is advantageous not only due to facile and low cost preparation but also because of improved bioavailability[8].

Two immiscible liquids can form a micro emulsion a single phase in which one of liquid is dispersed in the other forming micro sized aggregates that are

stabilized by a surfactant and co-surfactant, which lowers the interfacial tension between two liquids[9]. Micro emulsions represents a state intermediate between thermodynamically stable solution i.e micelles containing solubilized oils and ordinary emulsion which are relatively unstable[2].

Three types of micro emulsions are known depending on the composition[10]-

1. Oil in water type micro emulsion where oil droplets are dispersed in the continuous aqueous phase.
2. Water in oil type micro emulsions where water droplets are dispersed in the continuous oil phase.
3. Bi-continuous micro emulsions where micro domains of oil and water are inter-dispersed with in the system.

Micro emulsions also refers to an aqueous suspension of pseudo micelles which contain relatively hydrophobic lipid centers surrounded by a monolayer of amphipathic molecules bearing hydrophilic moieties.

Theories explaining the Formation of Micro Emulsions are[5]-

1 .interfacial or mixed film theory
2. Solubilization theory
3. Thermodynamic treatment theory

The bio-material was isolated from the fruit pulp of *manilkara zapota* by simplified economical method..three different escitalopram emulsions was formulated using bio stabilizer in different concentrations. The formulated emulsions were subjected for various evaluation parameters like globule size, ph, effect of centrifugation, viscosity, surface tension and rate of drug release. The formulated emulsions exhibit uniform globule size, promising stability against centrifugation effect in comparison to standard emulsion. The drug release studies from the formulated emulsions exhibited a promising stability, transparency, uniform globule size range, surface tension and sustainability for a period of 8 hours. Finally the conclusion was drawn that the isolated bio stabilizer acts as novel emulsifier for formulating various drug loaded micro emulsions.

Materials:

The model drug escitalopram was obtained from macloids laboratories ltd., mumbai as a gift sample. All the reagents were of analytical grade. Double distilled water was used throughout the experiment.

Isolation of the Bio-Polymer from *Manilkara zapota* Fruit pulp

The fruits of *manilkara zapota* were taken,peeled and mashed, the pulp was taken and weighed. 250gms of pulp was taken and to it was added 1000ml of double distilled water. The slurry was filtered using muslin cloth, a clear liquid was obtained and to it 500ml of methanol was added and was kept overnight in a refrigerator. The settled polymer was collected by filtration. The polymer was further dried and sieved through mesh size 120.the polymer obtained yields about 125mg.

Formulation of Escitalopram Micro-Emulsion using Bio-Polymer-

Three different microemulsions were prepared by the aqueous phase titration method. The optimized micro-emulsion mzm-1 was prepared by dissolving specified amount of drug in almond oil then co-surfactant was added in the mixture containing oil phase and drug, then sufficient quantity of distilled water is added to make the final preparation 100%w/w.(table no. 1)

Table no.1 Formulations prepared

Ingredients	Mzm-1	Mzm-2	Mzm-3
Almond oil(ml)	5	5	5
Distilled water (ml)	2.5	2.5	2.5
Drug (escitalopram) (mg)	40	40	40
Bio-polymer cp-1 (mg)	-	-	-
Bio-polymer cp-2 (mg)	40	80	120
Ethanol (ml)	7.5	18	23

Evaluation Parameters:

The dwarf emulsions were evaluated for the following parameters-

Globule size- The particle size was determined by optical microscopy method.

Viscosity- The viscosity of micro-emulsion was measured by using *ostwald viscometer*

Surface tension- The surface tension of micro-emulsion was measured using stalagmometer and was compared with sodium lauryl sulphate..

pH- The ph of dwarf emulsions was measured in digital ph meter using ph 7 as standard.

Content uniformity test - The content uniformity test is used to ensure that every dosage form contains the amount of drug substance intended with little variation within a batch. Due to increased awareness of physiological availability, the content uniformity test has been included in the monographs dosage forms intended for oral administration where the range of size of the dosage form available include 50mg or smaller sizes.

In case of emulsion and microemulsion 1ml of each was diluted with 19ml of alcohol and was subjected to orbital shaker for 30 mins.the mixture was taken and the content uniformity of drug was maesured.

In-vitro release studies- The in-vitro release studies in case of dwarf emulsions were performed using

dissolution apparatus for 8 hrs.the ph used was acidic for first 4hrs and was further replaced by alkaline ph.

Results and Discussions:

Physicochemical properties of the bio-material:

A novel bio-polymer from *manilkara zapota* was isolated by simplified economical process the yield was 1% per 100gms. The bio-polymer obtained was of brownish to dark brown color with a colour changing point of 146-150˚. The bio-polymer showed positive tests for the presence of proteins and carbohydrates. (table no.2, table no.3)

Table no.2 Physical properties of the bio-material

S.no.	Characteristic	Cp-2
1.	Colour	Brown
2.	Odour	Characteristic
3.	Taste	Sweet
4.	Melting point	146-150ºc

Table no.3 Chemical properties of the bio-material

S.no.	Chemical constituent	Cp-2
1.	Carbohydrates	Present
2.	Proteins	Present

Infra red spectra of the bio-polymer: The IR spectra of the bio-material was performed at mit, Meerut, UP., India.

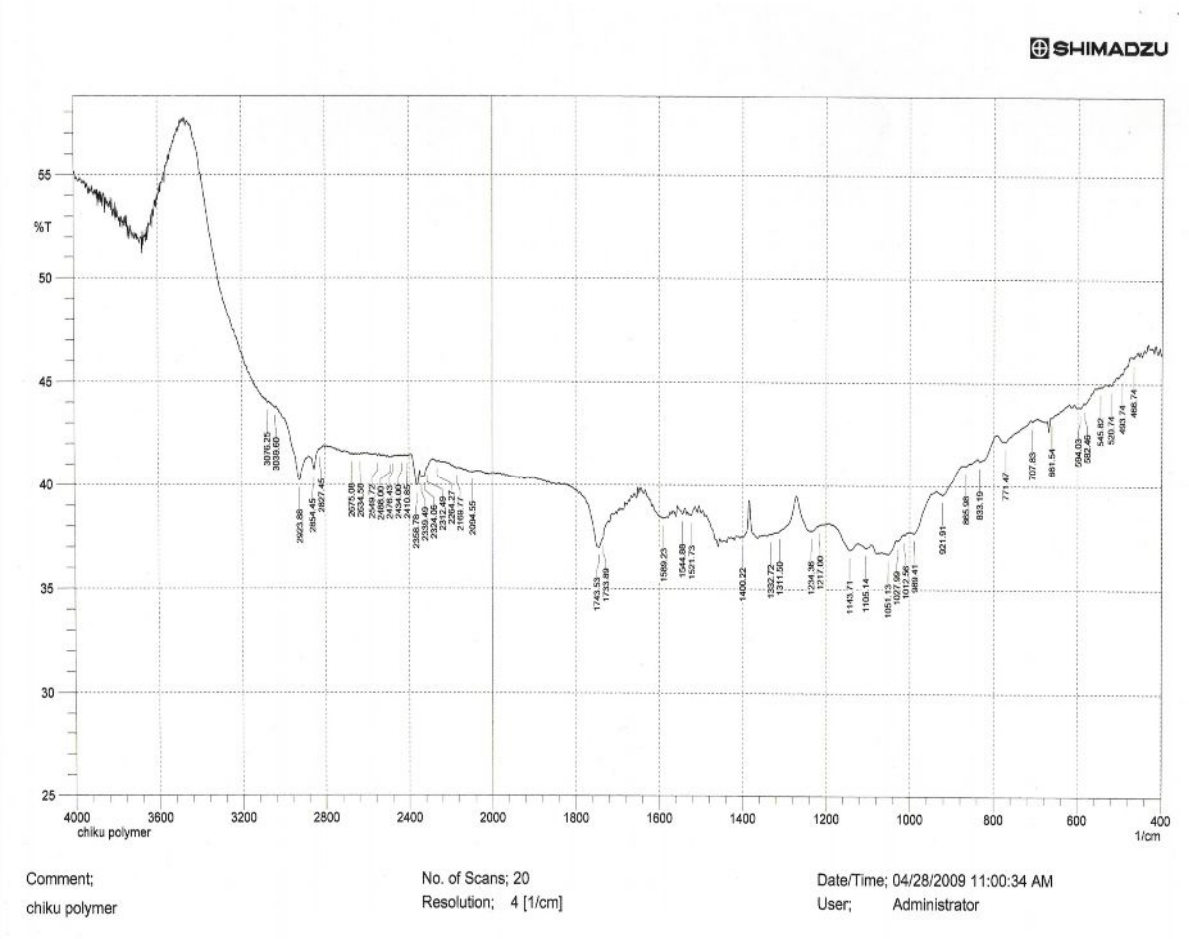

Fig. No. 1 infra red spectra of the bio-material

Evaluation Parameters:

Globule size and shape - the globules were observed to be spherical in shape with a size in the range 75-80 nm. (table no. 4)(fig. No. 2)

Content uniformity test- the content uniformity varied from 81.5% to 83% with formulation mzm-1 showing the highest content uniformity of 83%.(table no.4)(fig. No. 3)

***In-vitro* release studies-** the in-vitro release data in all the formulations was performed in zero order, zero-first order, higuchi equation in order to evaluate its release mechanism. The result showed the zero-first order release pattern.(fig. No. 4). Among the formulations, mzm-3 had a t50% and t80% of 3 and 5.5 hours respectively. (table no. 4).

Table no.4 Evaluation parameters

S.no.	Parameter	Mzm-1	Mzm-2	Mzm-3
1.	Viscosity(cps)	15.48	21.84	32.76
2.	Globule size	75nm	78nm	80nm
3.	Surface tension(dyne/cm)	63.29	61.18	57.35
4.	P h	6.58	6.67	6.77
5.	Content uniformity(%)	83%	81.5%	82%

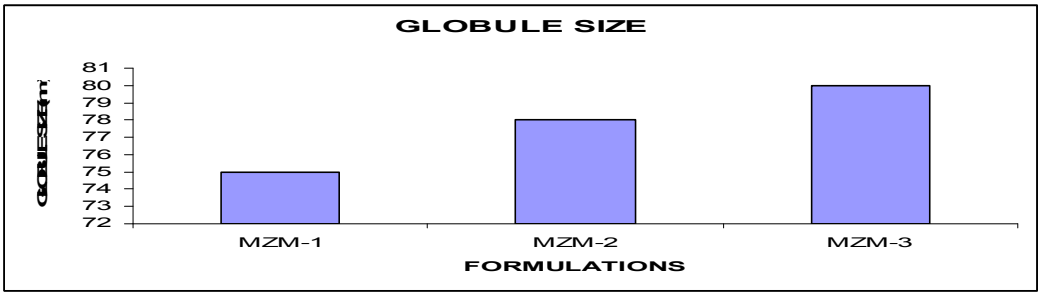

Fig. No. 2 globule size of microemulsions

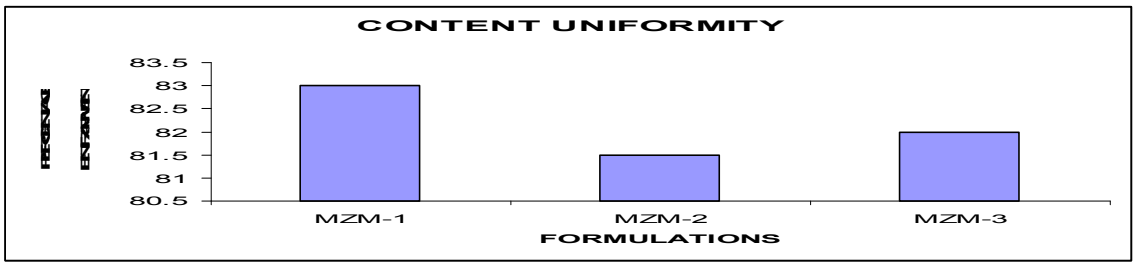

Fig. No. 3 content uniformity of microemulsions

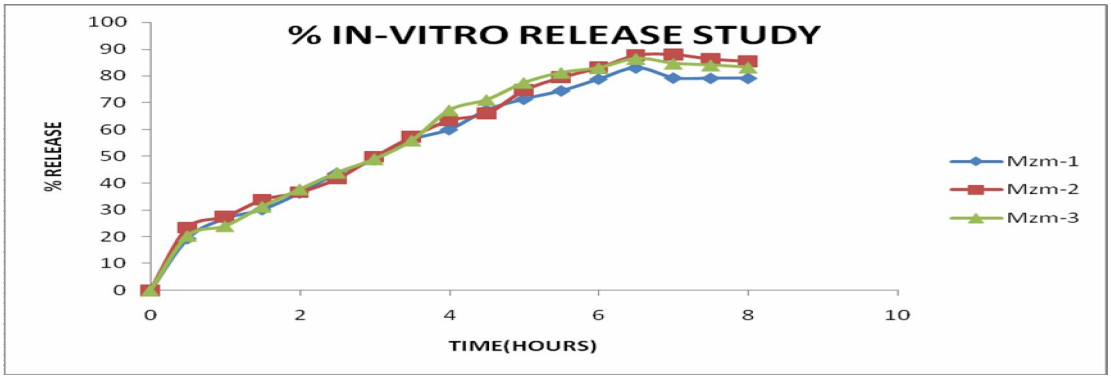

Fig. 4: *in-vitro* release study of the microemulsions of escitalopram.

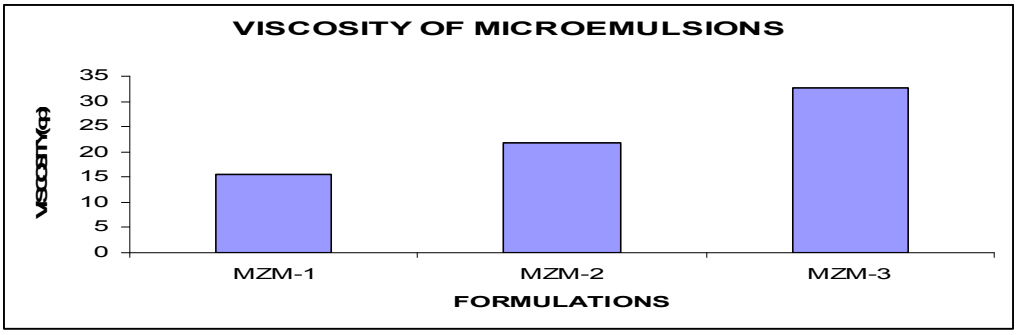

Fig. No. 5 viscosity of microemulsions

Discussions:

A novel bio-polymer from *manilkara zapota* was isolated by simplified economical processthe yield was 1% per 100gms.the bio-polymer obtained was of brownish to dark brown colour with a colour changing point of 146-150˚. The bio-polymer showed positive tests for the presence of proteins and carbohydrates. Three different formulations were formulated using various proportions of bio-material for the preparation of microemulsions of escitalopram. The in-vitro release data in all the formulations was performed in zero order, zero-first order, higuchi equation in order to evaluate its release mechanism. The result shows the zero-first order release pattern. The in-vitro release data in all the formulations was performed in zero order, zero-first order ,higuchi equation in order to evaluate its release mechanism. The result shows the zero-first order release pattern. Among the six formulations mzm-1 shows a globule size of 75nm, p h of 6.8, surface tension of 63.29 dyne/cm, viscosity of 15.48 cps. The t50 and t80 values were 3.1 hours and 6.2 hours respectively. The content uniformity was found out to be 83%.

Conclusion:

Finally the experimental results shown a promising observations in terms of globule size,content uniformity,stability,ph,viscosity and surface tension. Hence conclusion was drawn that the two isolated bio-polymers has shown its potentiality as bio-emulsifier for formulating emulsions and microemulsions. The polymer can serve as potential polymer for formulating various drug loaded emulsions.

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