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Development and evaluation of Pharmacosome formulations of Mefenamic acid

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Abstract

Patience who suffered from menstrual pain disease is generally prescribed the non-steroidal anti-inflammatory drug (NSAIDs). Monorrhagia or another blood disorder & some gynecological disorder, which impairs body function and acts as an economic burden. Due to respective use of ACE by oral route, it may cause GI complication such as bleeding, pain, perforation, abdominal pain, and swelling. To decrease the side effect of ACE, it is given by topical route in promotes the safety & efficacy of the ACE. The Mefenamic Acid pharmacosomes were prepared by the hand shaking method technique and evaluated by various methods such as in-vitro release study, % yield, drug entrapment efficiency, pH of the prepared formulation. The prepared system was also characterized by FTIR spectrophotometer to identify the drug-excipients interaction. The maximum entrapment efficiency of pharmacosomes was found to be 90%. The main aim of this study was to develop and characterized a vesicular drug carrier system for topical delivery of Mefenamic Acid to overcome the problem related with oral route.

Keywords: Pharmacosomes; Mefenamic Acid; Topical delivery; Monorrhagia; Gynecological disorder.

1. Introduction

Recently, researchers engaged the development of novel vesicular systems such as Liposomes, Niosomes, transfersome etc. Since the development of each has some of the advantages and some disadvantages. Newer systems developed with, a motive to overcome previous system disadvantage. So pharmacosome came in market with the new scientific approach. Oxidative degradation occurred in case of transfer some which can be overcome in case of pharmacosome [1-3]. A novel drug delivery system has been utilizing a lot in the past few years, and attention is also being paid to further develop this system [1,2].

Pharmacosomesdefined as “the colloidal dispersion of drug covalently bond to lipids, and many exist as an ultrafine vesicular micellae or hexagonal aggregates depending upon the chemical structure of drug-lipid complex.” The term “Pharmacosomes” derived from the two words i.e.pharmacon which means active principle & soma, carrier [3-5]. Pharmacosome are hexagonal complex of amphillic phospholipid & drug contains active H2 which bind to phospholipid complex. They also give better biopharmaceutical properties to drug which results to improved bioavailability. Pharmacosome already prepared for several NSAIDS, Cardiovascular, proteins &Anti neoplastic drugs. The objective of this delivery system is to target the drug at specific site during the time period of treatment as to produce the stable, efficacious and safe delivery system of Mefenamic Acid to overcome complications related to oral route by formulating the pharmacosomes of Mefenamic Acid for topical use. This delivery system is used in study because of their specialized characteristics and helps to incorporate the Mefenamic Acid efficiently and used as topically and ultimately reduce the oral side effects of Mefenamic Acid.

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1.1. Principle

The pharmacosome is based on principle, drug is bind with lipid covalently where compound resulting is a carrier & active compound at same time & the physicochemical properties depend on lipid &drug [6,7].

2. Material and methods

2.1. Materials

Mefenamic Acid was received as a gift sample from Syknokem Pharmaceutical, Haridwar, Uttrakhand, India. Soya lecithin, Methanol,Cholesterol,Mannitol,di-ethyl-ether,Poly vinyl Pyrollidone, Hydroxy Propyl Cellulose and Polyethylene glycol 400 were taken from Global Institute of Pharmaceutical education and research institute Kashipur Laboratory. All other materials and chemicals used were of either pharmaceutical or analytical grade.

2.2. Method

Perparation of topical drug-loaded Mefenamic acid Pharmacosomes was prepared by the hand-shaking method. (8-10) In this method, 3gm of mannitol powder and cholesterol in 3%, 2%, 4% and 5% were placed in 250ml RBf and held at a temp. of 70-80℃and also flask rotated at a speed of 85±5 rpm for 25-30 min in a rotatory evaporator [8,10].

Mefenamic Acid (50mg) and lecithin with a ratio of 0.1:1, 0.1:2, 0.1:3 and 0.1:4 was dissolved in methanol and di-ethyl ether in the ratio of 1:4 v/v and add 0.5ml aliquot of the above organic solution were introduced in RBF containing mannitol and cholesterol at 37℃After drying a second aliquot (0.5ml) of the solution was added and then dried, a thin film is formed on the surface of RBF and placed in a 230esiccators overnight and the sieved with 100 mesh. The Mefenamic Acid loaded Pharmacosomes were prepared and mentioned as f1, f2, f3, f4, f5 and f6 [11,12].

Table 1 Composition table of different formulation

Formulation code	Mefenamic acid(mg)	Methanol (ml)	Soya lecithin(gm)	Mannitol	Polyvinyl pyrrolidone (mg)	Cholesterol (%)	HPMC(mg)
F1	50	1	1	3	-	2%	20
F2	50	1	2	3	-	5%	-
F3	50	1	3	3	0.5	3%	-
F4	50	1	4	3	-	6%	10
F5	50	1	5	3	10	4%	-
F6	50	1	6	3	10	7%	10

2.3. Angle of repose

It can be determining the flow property of powder. Generally, the higher is the angle of repose poor is the flowability of powder. This method is used in glass funnel method[13,14]. The formula is:

$$tan\emptyset = \frac{h}{r}$$

Therefore,

Ø= Tan-1 (h/r)

so,

$$\emptyset = Angle\ of\ repose$$

h = Cone height

r = Cone radius made by blend of powder

2.4. Tapped Density

It is also determining the flowability & geometry. It is determined by tapping using weighed the sample amount in measuring cylinder[15,16]. The formula is-

$$\rho t = \frac{M}{Vt}$$

Where,

$$\rho t = tapped\ density$$

M = Powder weight

Vt = Tapped powder

2.5. Density of bulk

Bulk density was detected by pouring preseived (#40 plexus) powder into the graduated cylinder by a large funnel & measuring its weight & vol[17,18].

It was calculated in the form of gm/cm3 and the formula is-

$$Bulk\ density = \frac{Mass\ of\ the\ sample}{Bulk\ volume}$$

$$Bulk\ Density\ (\delta 0) = M/V0$$

M= Sample mass or sample weight

V= Apparent vol. or Bulk volume

2.6. Carr'sIndex

It is determined by the uniformity of the weight[19].

$$Carr's\ Index = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} \times 100$$

2.7. Ratio of Hausner's[13]

The ratio less than 1.25 denotes good flow and < 1.5 denotes poor flow[20]. The formula is given by:

$$Hausner's\ Ratio = \frac{tapped\ density}{bulk\ density}$$

$$Hausner's\ ratio = (\delta t/\delta 0)$$

$$\delta t = Tapped\ density$$

$\delta 0$= Bulk density

2.8. Analysis of solubility

The Mefenamic acid solubility determined in a set of solvents (methanol, water, Ethanol). A small amount of solvent (upto 1-5ml) was placed in a test-tube and then the small amount of drug was added and the solution was kept overnight for complete solubilization. After that, the solution was sonicated for 5 min and then t 0.1ml of solution was pipette out from the test tube and then preparation of further dilutions & absorbance was determined by the UV Spectrophotometer against with a blank solution. The drug amount which is soluble was calculated with the calibration curve equation [21].

2.9. Determination of melting point

The determination of melting point was performed for determining the drug purity, if there is any impurity found that the melting point range deviates from its original readings. Mefenamic acid melting point was determined by the usage of m.p apparatus, drug is filled (amount of sample) in capillary tube &it's one end sealed with the help of flame and placed apparatus pocket which is attached with thermometer. This process started & that point where the drug starts melts was noted [15].

2.10. Moisture Content determination

The preparations were subjected for studying moisture content by using an IR moisture balance and then placingpharmacosome at 105ºC for 10min [16].

3. Results and discussion

Table 2 Flow properties of Mefenamic acid (powder)

S. No.	Powder properties	Results			
		F1	F2	F3	F4
1	Bulk density	0.495±0.03	0.497±0.02	0.491±0.01	0.499±0.02
2	Tapped density	0.522±0.05	0.524±0.04	0.52±0.08	0.526±0.07
3	Angle of repose	30±0.02	30.2±0.05	30.11±0.03	30.15±0.06
4	Carr's index	27.30±0.07	27.34±0.03	27.31±0.06	27.32±0.01
5	Hausner's ratio	1.40±0.04	1.43±0.02	1.41±0.09	1.46±0.05

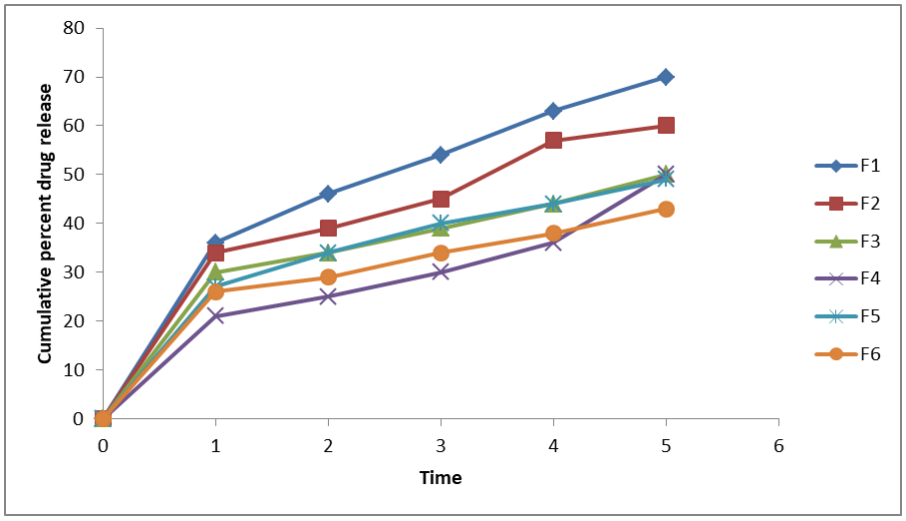

Figure 1 Release profile of different formulations

Preformulation study of mefenamic acid was done by placing the following test:-

That is drug solubility, drug melting point; flow property was done according to Indian Pharmacopoeia.The Organoleptic properties of pharmacosome was observed by physical & visual method, the properties were matched with the std. drug & the prepared mefenamic acid pharmacosome was non sticky in appearance.The solubility of mefenamic pharmacosome was matched with the standard drug. The mefenamic acidpharmacosome melting point was found to be 230.2ºC and standard range is 230º-231ºC

Angle of repose was found to be 30 it indicates that the powder is passable. Bulk density was found to be 0.495 having good flow property. Tapped density was found to be0.522. The *in-vitro* drug release study was done in USP XIII

dissolution test apparatus type II. In this, temperature was set at 37ºC ±5ºC & set at 50rpm. The phosphate buffer of 1000 ml was set for 12 hr. The release of drug at diff. time interval has been analyzed by UV spectrophotometer at 285nm.

4. Conclusion

In this study, it has been concluded that the formulation of Mefenamic acid pharmacosomes provides the sustained action of the drug. The Mefenamic acid Pharmacosomes were successfully formulating by using cholesterol, mannitol, di-ethyl ether for topical use. In this, the polymer used as a carrier of Mefenamic acid drug release. The Mefenamic acid pharmacosomes have a capability to penetrate the lipoidal structure easily & produce a prolonged action. When the Mefenamic acid given orally, it will produce the GI complication so, to overcome this, the topical preparation of Mefenamic acid pharmacosome can be formulated; it is used in the treatment of Monorrhagia or another blood disorder & some gynecological disorder.

Therefore, it was concluded that the formulation could be very promising alternative for the topical or transdermal treatment.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest.

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