INTERNATIONAL JOURNAL OF DRUG DISCOVERY AND HERBAL RESEARCH (IJDDHR)
13(3):July.-Sept.: (2023), 49-55
ISSN: 2231-6078

Research Article

Formulation and Evaluation of a Novel Drug Delivery System of Aceclofenac for Colonic Drug Delivery

Ms Neetu Kori, Dr Reetesh Yadav.

Shriram Institute of Pharmacy, Jabalpur, M.P., India

Abstract

In the present study a formulation method was developed and *in-vitro* characterization of sodium alginate and cellulose acetate phthalate based microspheres were prepared for colonic delivery, where sodium alginate act as a natural polymer based carrier which is inexpensive and also having hydrophilic properties. The aceclofenac microspheres were prepared and optimized formulation on the basis of entrapment efficiency and drug release study. The highest and lowest drug content was found to be MF_1 (88.72±0.92%) and MF_{12} (45.79±0.28) respectively. The percentage yield and entrapment efficiency was increased by increasing the ratio polymer and coating ratio.

In-vitro aceclofenac release study of sodium alginate microspheres coated with CAP was performed in SGF and the minimum drug release was found to be MF_{12} (1.37±0.02%) to MF_{14} (2.46±0.06%) because of CAP polymer not dissolve in acidic medium in these formulation CAP using as coating agent that is 9%. So the formulation MF_{12} and MF_{14} are minimum drug release in the SGF and these formulations are the best formulation for colonic delivery

Keywords: Microspheres ,aceclofenac, sodium alginate, sodium alginate, drug content ect.

Introduction :

1. In the area of targeted delivery, the colonic region of the GI tract is the one that has been embraced by scientists and is being extensively investigated over the past two decades. Targeted delivery to the colon is being explored not only for local colonic pathologies, thus avoiding systemic effects of drugs or inconvenient and painful trans-colonic administration of drugs, but also for systemic delivery of drugs like proteins and peptides, which are otherwise degraded and/or poorly absorbed in the stomach and small intestine but may be better absorbed from the more benign environment of the colon[1-3]

The treatment of disorders of the large intestine, such as irritable bowel syndrome (IBS), colitis, Crohn's disease and colon disease, where it is necessary to attain a high concentration of the active agent, may be efficiently achieved by colon-specific delivery. The necessity and advantages of a colon-specific drug delivery system (CDDS) have also been extensively reviewed elsewhere in the literature[4-7].

There are various approaches in delivering a therapeutics substance to the target site in a controlled fashion. One such approach is polymeric microspheres as drug carriers.

Microspheres based on drug delivery system have received considerable attention. The most important characteristic of microsphere is the microsphere separation morphology which endows it with a controllable variability in degradation rate and also drug release.[8]

Materials and Methods[6-13]

Preparation of Aceclofenac microspheres:

Aceclofenac microspheres were prepared by ionic gelation method. Here, required amount of sodium alginate was dispersed in a specified volume of cold water allowed to swell for 2 hours. In another beaker required amount of drug was dispersed in phosphate buffer pH 7.4 solution. The drug solution was added to sodium alginate solution with stirring to produce a viscous form. The drug polymer solution was added drop wise by using syringe of 22 G in diameter form a height of about 5cms into a beaker containing 4% w/v solution of calcium chloride with continuous stirring by magnetic stirrer. Then the solution was containing microspheres was filtered by filter paper. The microspheres were allowed to dry at about 30 to 40^{0}C and it is coated with cellulose acetate phthalate. Cellulose acetate phthalate was dissolve in 50% acetone and 50% ethanol solution and this solution is used as a coating solution. Sodium alginate microspheres was poured in the coating solution by continuous stirring then the solution was evaporated and coated cellulose acetate phthalate microspheres was prepared and it is stored in well-closed container. [9-12]

Optimized formula:

The formula was optimized on the basis of higest drug content and drug release study. The following formula was optimized.

Corresponding Author

E.mail: shailgpharma@gmail.com

Table. 1 Optimized formula for aceclofenac microsphers

Sl. No.	Formulation code	Aceclofenac (Ratio)	Sodium alginate (Ratio)	Cellulose acetate pthalate (%)
1	MF_1	1	1	5
2	MF_6	1	1.50	9
3	MF_9	1.25	1.50	7
4	MF_{10}	1.25	0.75	7
5	MF_{11}	1.25	2	7
6	MF_{12}	1.25	2	9
7	MF_{13}	1	1	7
8	MF_{14}	1	1	9

Characterization of Aceclofenac microspheres:[10-14]

The aceclofenac microspheres were characterized on the following parameters.

Appearance:

The microspheres formed were white to off-white in color, spherical in shape and free flowing in nature.

Yield calculation :

The prepared microspheres were assessed for the yield value. The batch was weighed after total drying and the yield % was calculated using the formula give below.

$$\text{yield } \% = \frac{W_{MF}}{W_C} \times 100$$

Where, W_{MF} = Weight of the prepared microspheres

W_C = Charge weight.

Determination of Micromeritic Properties of Prepared Microspheres:

- **The particle size distribution of microspheres :**

The microspheres were subjected to granulometric study using a standard ASTM Sieve [American Society for testing and materials] set comprising of a nest of sieves ranging from # 22 to # 44 mesh ASTM(having apertures 710 to 355 micron]. The microspheres were sieved for around 10minutes by mechanical sieves shaker (Cuprit Electrical Co. India). Then the particles retained on each sieve were weighed and % retained on each sieve was calculated.

Mean particle size determination:

The mean particle size of each formulation was determined using the following formula

$$\text{Mean particle size} = \frac{\sum(\text{mean particle size of fraction x weighed fraction})}{\sum(\text{weight fraction})}$$

- **Flow properties of prepared microspheres :**

Flow properties of prepared microspheres were determined by bulk density, tapped density, Carr's index and Hausner Ratio or Packing factor.

- **Determination of bulk density and tapped density :**

An accurately weighed quantity of drug crystals and prepared microspheres were carefully poured into the graduated cylinder (10ml). The initial volume was measured. The graduated cylinder was tapped for 100 times. After that the volume was measured.

$$\text{Bulk Density} = \frac{W}{V_O}$$

$$\text{Tapped Density} = \frac{W}{W_F}$$

Where W = weight of the formulation

V_O = Bulk Volume

W_F = Tapped Volume

Bulk and Tapped density expressed in gm/ml.

- **Carr's index or compressibility index :**

$$\text{Carr's index} = \frac{\text{Tapped density - bulk density}}{\text{Tapped density}} \times 100$$

Grading of the powders for their Flow properties according to the Carr's index.

Hausner ratio:

It indicates the flow properties of the powder and measured by the ratio of tapped density to bulk density.

$$\text{Hausner Ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Drug content analysis of prepared microspheres:

Microspheres were crushed and powdered by using a mortar. Accurately weighed 100 mg of this powder was taken in a 10ml volumetric flask and make the volume with PBS pH 7.4.The flask was stopped tightly and kept on mechanical shaker for 24hr.Then the solution was added to 10 ml more PBS solution. Then solution was filtered through whatmen filter paper. From the filtrate 1ml solution was diluted to 10ml with PBS pH 7.4 in a 10ml volumetric flask, and from the above solution 1 ml was diluted to 10ml with PBS pH 7.4 in a 10ml volumetric flask, then the diluted solution was assayed in UV-VIS Spectrophotometer [Shimadzu-1800] at 274.0nm to find out the Aceclofenac content of microspheres. The drug content or entrapment efficiency were calculated from the observed data[13].

***In-vitro* drug release study in simulated gastrointestinal fluids:**

Sodium alginate and cellulose acetate phthalate coated aceclofenac microspheres were valuated or the in vitro drug release in simulated GI fluids (SGF). The release studies were performed in SGF pH 1.2. The temperature of the dissolution medium was set and thermostatically controlled and maintained at 37± 0.5^{0}C. The volume of the dissolution fluids taken was 900ml SGF pH 1.2. The agitation speed was kept fixed at 50 rpm throughout the study. Microspheres of 100 mg Aceclofenac in a capsule was taken in the basket type of the dissolution apparatus.5 ml samples were with drawn from the dissolution medium at different time intervals and equivalent volume 5 ml of fresh dissolution medium was added. The sampling time were in 30 minutes interval withdrawn 5ml samples were placed in beaker and filter the solution 1ml from these solution withdraw and diluted upto 10 ml with SGF. These samples were analyzed in spectrophotometrically by UV- 1800 (Shimadzu)] at 274.0 nm and using standard curve equation, the amount of drug release was calculated by Computer excel program.These study was performed for 2 hours and further release profile was studied in SIF[13].

Surface morphology:

The sample for the SEM analysis was prepared by sprinkling the microspheres on one side of a adhesive stub. Then the microspheres were coated with gold before microscopy. Finally the microspheres were observed with the scanning electron microscope[13-14].

Result and Discussion

The aceclofenac microspheres were characterized on the following parameters.

Appearance:

The microspheres formed were white to off-white in color, spherical in shape and free flowing in nature.

Yield Calculation:

The percentage yield of various formulation was shown in the following table.

From the above table the percentage yield was found to be in formulation MF_1, MF_6, MF_9, MF_{10}, MF_{11}, MF_{12}, MF_{13} and MF_{14} highest due to increasing the polymer ratio and percentage entrapment efficiency was found to be highest in formulation MF_1, MF_6, MF_9, MF_{10}, MF_{11}, MF_{12}, MF_{13} and MF_{14} highest due to increasing the polymer ratio. (table no.2)

Determination of micromeritic properties of prepared microspheres:

The micromeritics data was shown in the following table.

From the above table the bulk density values ranged between 0.476±0.002 to 0.681±0.003 gm/ml and tapped density values ranged between 0.480±0.003 to 0.714±0.002gm/ml. The result of Carr's Index range from 2.08±0.02% to 10.09±0.062%, suggest excellent flow characteristics of the microspheres. Hausner's ratio from 1.02±0.02to 1.08±0.02 which shows that the aceclofenac microspheres good flow properties.

In above figure the MF_4 formulation shows maximum release in SGF and minimum release in MF_1 and MF_4 due to coating ratio and polymer concentration. So the MF_1 formulation was optimized formulation because the minimum drug release shown in stomach in colonic delivery.

In above figure the MF_7 formulation shows maximum release in SGF and minimum release in MF_5 and MF_6 due to coating ratio and polymer concentration. So the MF_6 formulation was optimized formulation because the minimum drug release shown in stomach in colonic delivery.

In above figure the MF_9,MF_{10} and MF_{11} formulation shows maximum release in SGF 2.20±0.04% due to coating ratio and polymer concentration. So these formulation was optimized formulation because the minimum drug release shown in stomach in colonic delivery.

In above figure the MF_{12}, MF_{13} and MF_{14} formulation shows maximum release in SGF 2.46±0.19% due to coating ratio and polymer concentration. So these formulation was optimized formulation because the minimum drug release shown in stomach in colonic delivery.

Scanning Electron Microscopy study:
Scanning electron microscopy was used to observe the surface morphology of cellulose acetate phthalate coated sodium alginate microspheres with drug. The scanning electron microscopy shows smooth surface of the microspheres and particle size was found to be 500 µm.
.

Reference

1. Okabes, Takeuchi, Kumini H, Kanno M, Kawashima M, Rig Dis. Sci,1983; 28:1034.
2. Rubinstein A, "Approaches and opportunities in colon specific drug delivery", Drug Carrier Syst.1995;12:101–149.
3. Tozer T R, Friend D R, McLeod A D, "Kinetic perspectives on colonic delivery", S T P Pharma Sci.1995;5:5–28.
4. Conchie J, Macleod D C, "Glycosidase in mammalian alimentary tract", Nature. 1959;184:233.
5. Kinget R, Kalala W, Vervoort L, Mooter G, "Colonic drug targetting", J Drug Target. 1998;6:129–149.
6. Watts P J, Illum L, "Colonic drug delivery", Drug Dev Ind Pharm. 1997;23: 893–913.
7. Yang L, Chu J S, Fix J A, "Colon specific drug delivery: new approaches and in vitro/in vivo evaluation", Int J Pharm.2002;235: 1–15.
8. Jain N.K. Text Book of Controlled and Novel Drug Delivery System.1997; 236-251.
9. Sunil K. Jain,Gopal Rai,D. K. Saraf, and G.P.Agrawal "Preparation and evaluation of albendazole microspheres for colonic delivery",Pharmaceutical Technology DECEMBER 2004;66-71.
10. M. K. Chourasia, S. K. Jain "Review on pharmaceutical approaches to colon targeted drug delivery systems", J Pharm Pharmaceut Sci.2003;6(1):33-66.
11. Krishnaiah YSR, Seetha Devi A, Nageswara Rao L, Bhaskar Reddy PR, Karthikeyan RS, Satyanarayana V "Guar gum as a carrier for colon specific delivery; influence of metronidazole and tinidazole on *in vitro* release of albendazole from guar gum matrix tablets", J Pharm Pharmaceut Sci (www.ualberta.ca/~csps). 2001;4(3):235-243.
12. Ravi P., Kusumanchi R.M, Malikarjun V., Baby rao B and Narendra B.R. "Formulation and evaluation of Gaur gum microspheres of aceclofenac for colon targeted drug delivery". J. of Pharmacy Research.2010;3(7):1510-1512.
13. Indian Pharmacopoeia Government of India ministry of health and family welfare. The Controller of Publication, Delhi.2007;1:143.
14. Umadevi S.K, Thiruganesh R. and Suresh S. Preparation and characterization of Chitosan tablets of aceclofenac for colon targeted drug delivery. JPRHC.2010;2(1):46-65.

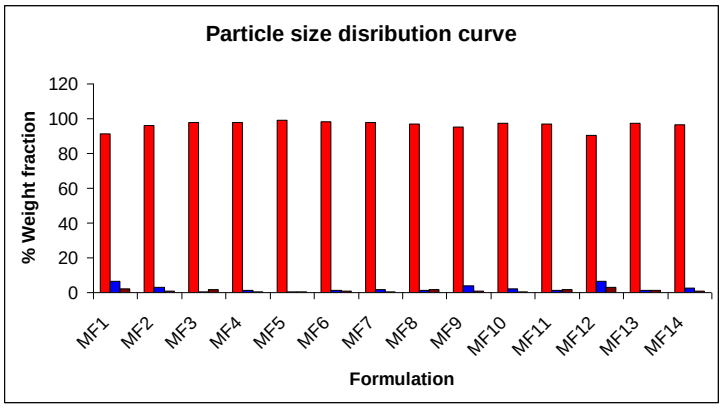

Fig 1: Particle size distribution curve of various formulations

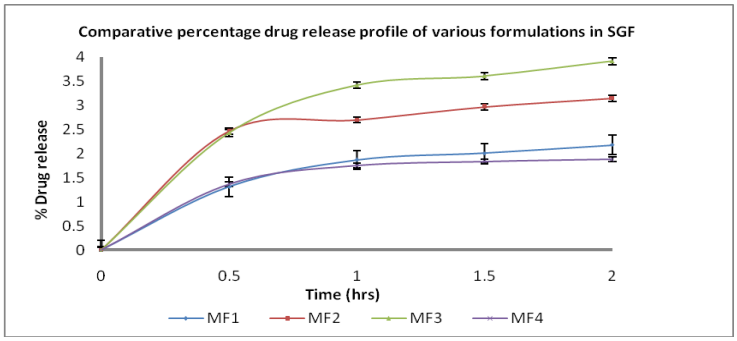

Fig 2 : Comparative drug release profile of MF_1, MF_2, MF_3 and MF_4 in SGF

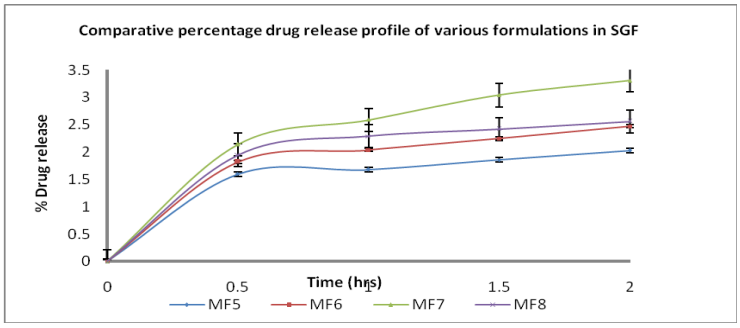

Fig 3 : Comparative drug release profile of MF_5, MF_6, MF_7 and MF_8 in SGF

Table 2 :Percentage yield and percentage entrapment calculation of arious formulations

Sl. No.	Formulation code	Drug: Polymer	Percentage Yield	Percentage Encapsulation Efficiency
1	MF_1	1:1	96.21 ± 0.14	88.72±0.92
2	MF_2	1:1.5	98.35 ± 0.12	73.46±0.29
3	MF_3	1:2	88.42 ± 0.15	55.97±0.73
4	MF_4	0.75:1	98.13 ± 0.19	75.41±0.43
5	MF_5	1.25:1	96.17 ± 0.20	58.18±0.36
6	MF_6	1:1.50	97.43 ± 0.12	58.79±0.60
7	MF_7	1:1.50	97.24 ± 0.29	38.21±0.54
8	MF_8	0.75:1.50	94.17 ± 0.20	51.09±.078
9	MF_9	1.25:1.50	97.26 ± 0.04	74.42±0.80
10	MF_{10}	1.25:0.75	97.03±0.24	64.01±0.43
11	MF_{11}	1.25:2	91.27 ± 0.12	61.58±0.33
12	MF_{12}	1.25:2	89.93 ± 0.09	45.79±0.28
13	MF_{13}	1:1	91.11 ± 0.07	51.27±0.72
14	MF_{14}	1:1	95.45 ± 0.06	50.92±0.30

Table 3 : Data for Bulk density, Tapped density, Carr's index and Hausner's ratio.

Formulation code	Bulk Density (in gm/ml)	Tapped Density (in gm/ml)	Carr's Index (in %)	Hausner's Ratio
MF_1	0.490±0.007	0.480±0.003	2.08±0.02	1.02±0.02
MF_2	0.476±0.002	0.50±0.02	5.04±0.032	1.05±0.15
MF_3	0.490±0.005	0.510±0.002	4.08±0.050	1.04±0.01
MF_4	0.487±0.001	0.512±0.002	5.13±0.025	1.05±0.01
MF_5	0.512±0.002	0.526±0.001	2.70±0.061	1.02±0.03
MF_6	0.487±0.002	0.512±0.002	5.13±0.025	1.05±0.02
MF_7	0.526±0.002	0.555±.0.002	5.60±0.041	1.05±0.01
MF_8	0.512±0.003	0.526±0.003	2.73±0.015	1.02±0.01
MF_9	0.540±0.001	0.571±0.001	5.82±0.03	1.05±0.03
MF_{10}	0.535±0.002	0.576±0.001	7.66±0.025	1.07±0.01
MF_{11}	0.576±0.002	0.625±0.002	8.50±.025	1.08±0.01
MF_{12}	0.545±0.002	0.60±0.02	10.09±0.062	1.10±0.01
MF_{13}	0.625±0.002	0.681±0.003	3.5±0.3	1.08±0.02
MF_{14}	0.681±0.003	0.714±0.002	4.84±0.045	1.04±0.02

Table 4: Particle size distribution data:

Formulation Code	% Yield	Weight % retention in different ASTM Sieve		
		710µm	500 µm	355 µm
MF_1	96.21 ± 0.14	91.11±0.96	6.66±0.43	2.22±0.02
MF_2	98.35 ± 0.12	96.15±0.25	3.10±0.16	0.77±0.07
MF_3	88.42 ± 0.15	97.92±0.86	0.51±0.01	1.55±0.04
MF_4	98.13 ± 0.19	98.04±0.70	1.46±0.16	0.48±0.02
MF_5	96.17 ± 0.20	99.11±0.72	0.44±0.01	0.44±0.02
MF_6	97.43 ± 0.12	98.17±0.31	1.09±0.01	0.72±0.02
MF_7	97.24 ± 0.29	97.76±0.84	1.78±0.14	0.44±0.02
MF_8	94.17 ± 0.20	96.86±0.39	1.34±0.04	1.79±0.03
MF_9	97.26 ± 0.04	95.37±0.62	3.70±0.23	0.92±0.02
MF_{10}	97.03±0.24	97.23±0.17	2.20±0.02	0.55±0.04
MF_{11}	91.27 ± 0.12	96.79±0.17	1.28±0.02	1.92±0.01
MF_{12}	89.93 ± 0.09	90.57±0.28	6.52±0.25	2.89±0.07
MF_{13}	91.11 ± 0.07	97.59±.31	1.20±0.03	1.20±0.02
MF_{14}	95.45 ± 0.06	96.66±0.15	2.66±0.07	0.67±0.02

Table5 : Comparative percentage drug release profile of various formulations in SGF

Drug release profile of various formulations in SGF (%)														
Time (hrs)	MF_1	MF_2	MF_3	MF_4	MF_5	MF_6	MF_7	MF_8	MF_9	MF_{10}	MF_{11}	MF_{12}	MF_{13}	MF_{14}
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.5	1.31 ±0.02	2.47 ±0.06	2.43 ±0.07	1.37 ±0.05	1.60 ±0.04	1.82 ±0.03	2.14 ±0.03	1.95 ±0.05	1.37 ±0.04	1.10 ±0.10	1.29 ±0.04	1.75 ±0.03	0.84 ±0.02	0.86 ±0.03
1	1.87 ±0.20	2.70 ±0.04	3.42 ±0.04	1.75 ±0.02	1.68 ±0.02	2.04 ±0.02	2.59 ±0.21	2.29 ±0.21	1.51 ±0.05	1.17 ±0.02	1.63 ±0.04	2.0 ±0.15	1.06 ±0.03	1.05 ±0.04
1.5	2.01 ±0.03	2.97 ±0.04	3.61 ±0.03	1.84 ±0.03	1.86 ±0.03	2.25 ±0.03	3.04 ±0.04	2.42 ±0.03	1.63 ±0.03	1.37 ±0.04	1.92 ±0.03	2.20 ±0.05	1.19 ±0.02	1.18 ±0.03
2	2.18 ±0.01	3.15 ±0.02	3.92 ±0.05	1.88 ±0.03	2.03 ±0.04	2.47 ±0.03	3.31 ±0.03	2.56 ±0.03	1.74 ±0.03	1.51 ±0.02	2.20 ±0.04	2.46 ±0.19	1.41 ±0.10	1.27 ±0.04

± S.D. (n=3)

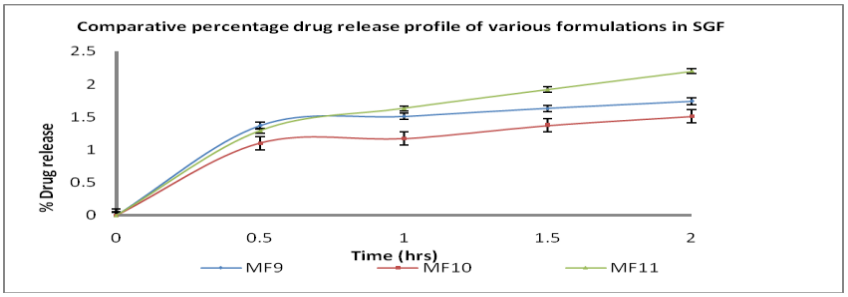

Fig 4 : Comparative drug release profile of MF_9 MF_{10}, and MF_{11} in SGF

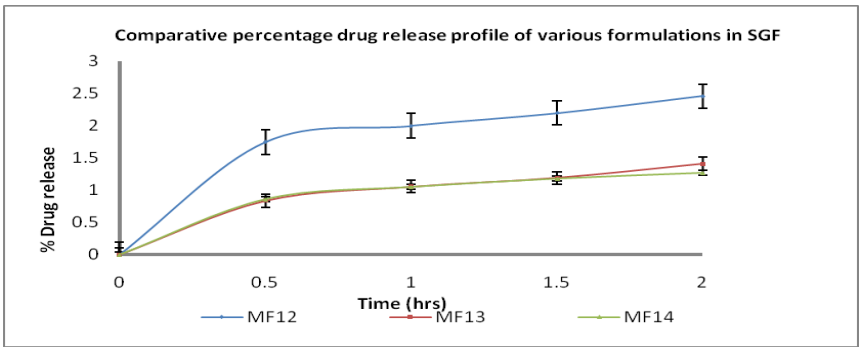

Fig 5: Comparative drug release profile of $MF_{12}MF_{13}$, and MF_{14} in SGF

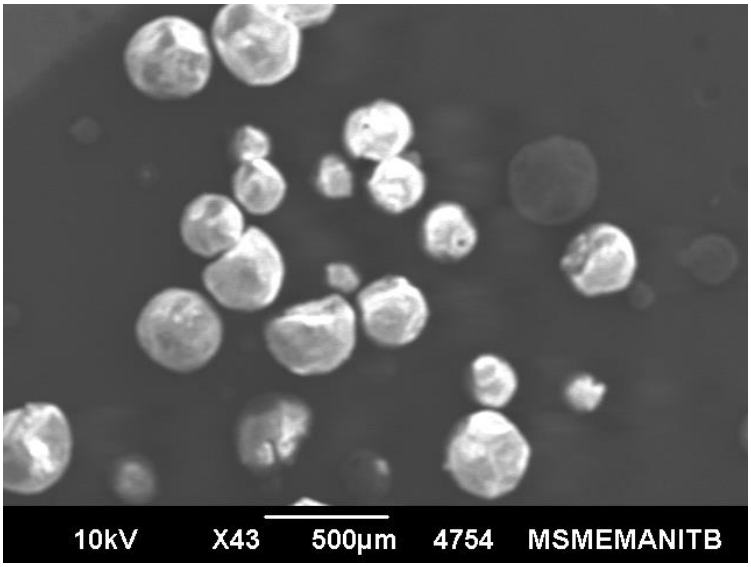

Fig 6: SEM image of MF_1 formulation