WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 5, 1151-1157. Research Article ISSN 2277– 7105

INVITRO WASSH OFF COMPARISION STUDIES OF SODIUM ALGINATE MUCOADHESIVE MICROSPHERES USING DIFFERENT POLYMERS

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Article Received on
06 March 2016,

Revised on 26 March 2016,
Accepted on 15 April 2016

DOI: 10.20959/wjpr20165-6136

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ABSTRACT

The aim of present work is to prolong the gastric residence time of microspheres by formulating into mucoadhesive control release microspheres. The mucoadhesive microspheres were prepared by ionotropic gelation method of polyelectrolyte complexation technique using sodium alginate as control release polymer and carbopol934, hydroxy propyl methyl cellulose, methyl cellulose, tragacanth, sodium carboxy methyl cellulose as mucoadhesive polymers in different proportions and calcium chloride as agent of multivalent cations. The prepared microspheres were characterized by micrometric properties, mean particle size, invitro wash-off test. The data obtained in this study suggests that a micro particulate mucoadhesive dosage forms can be successfully formulated to give prolonged residence time.

KEYWORDS: gastric residence time, sodium alginate, carbopol 934, inotropic gelation method.

INTRODUCTION

Microspheres are defined as solid colloidal approximately spherical shape particles size ranging from 1µm to 1000 µm in diameter. However, the success of these microspheres is limited due to their short residence time at site of absorption. To overcome this limitation the microspheres are coupled with mucoadhesion character by incorporating mucoadhesive polymers into their formulation to develop mucoadhesive microspheres. Mucoadhesion is the attachment of the drug along with a suitable carrier to the mucosal layer. Mucoadhesion is a complex phenomenon which involves wetting, adsorption and interpenetration of polymer chains.

The mucoadhesive microspheres are formulated by using mucoadhesive polymers, these mucoadhesive polymers have the property of adhering to mucin epithelial surface. A short list of Mucoadhesive polymers is given in Table no. 1.

MATERIALS

Sodium alginate, carbopol 934, hydroxy propyl methyl cellulose, methyl cellulose, sodium carboxy methyl cellulose and calcium chloride received from Himedia laboratories.

METHOD

mucoadhesive microspheres were prepared by ionotropic gelation method using polyelectrolyte complexation technique. In this method the required amount of sodium alginate, mucoadhesive polymer and calcium chloride were weighed and passed through sieve no ≠ 60. Sodium alginate and mucoadhesive polymer was dissolved in water to form a homogenous polymer solution by continuous stirring. The resultant dispersion was loaded into dry disposable syringe with needle size no 20 and added drop wise into 2% w/v solution of calcium chloride under constant stirring. The added droplets were retained in the calcium chloride solution for 15 min to complete the curing reaction and to produce the spherical rigid microspheres. The microspheres were collected by decantation, and the product thus separated was washed repeatedly with water and dried at room temperature for 24 hours. Total 7 formulations were prepared by using different polymer ratios, are listed in table 2.

Table no. 1: **list of Mucoadhesive polymers**

Synthetic polymers	Natural polymers
Cellulose derivatives	Tragacanth
polycarbophil	Sodium alginate
Poly (ethylene oxide).	Karaya gum
Poly (vinyl pyrrolidone).	Guar gum
Poly (vinyl alcohol).	Gelatin
Poly (hydroxyethyl methylacrylate)	Chitosan
Hydroxyl propyl cellulose	Soluble starch
Poly ethylene oxide	Xantham gum
Methyl cellulose (MC)	Lecithin

Table 2: composition of different formulations.

SL.NO	BATCH CODE	POLYMERS	RATIO/GRAMS
1.	B1	Sodium alginate	2g
2.	B2	Sodium alginate : Carbopol 934	1.8 : 0.2
3.	B3	Sodium alginate : CMCNa	1.8 : 0.2
4.	B4	Sodium alginate	4g
5.	B5	Sodium alginate : Carbopol 934	2 : 2
6.	B6	Sodium alginate : Methyl cellulose	2 : 2
7.	B7	Sodium alginate : HPMC	2 : 2

EVALUATION METHODS

Micromeritic properties: The prepared mucoadhsive microspheres were characterized by their micromeritic properties such as particle size, bulk density, tapped density, compressibility index Hausner's ratio and angle of repose.

A)Tapped density: The prepared mucoadhesive microspheres were transferred to a graduated cylinders of bulk density apparatus and the tapping was set for 100 times. After 100 tappings, volume of microspheres was visually examined. The ratio of weight of microspheres to volume of microspheres after 100 tappings gives tapped density.

Tapped density= Mass of microspheres in grams / Voiume of microspheres after 100 tapping

B) Bulk density: The prepared mucoadhesive microspheres were transferred to a graduated cylinder of bulk density apparatus and the volume occupied by the microspheres was noted. This volume is bulk volume and it includes true volume of the power and the void space among the microspheres.

Bulk density = Weight of microspheres in grams/ Bulk volume of microspheres in cm^3

C) Carr's compressibility index: The compressibility index is a measure of flow of a powder to be compressed. It was determined by using the bulk and tapped densities.

Carr's compressibility index = Tapped density- Bulk density x100/Tapped density

D) Hausner's ratio: Tapped density and bulk density were measured and the Hausner's ratio was calculated using the following formula:

Hausner's Ratio = Tapped density/Bulk density

The values less than 1.25 indicate good flow where as greater than 1.25 indicates poor flow.

E) Angle of repose: Angle of repose is defined as the maximum angle possible between the surface of the pile and the horizontal plane, which can be deterined by using fixed funnel

method. In fixed funnel method a funnel was set with its bottom tip at a given height (h) above a graph paper which is placed on a flat horizontal platform.

Accurately weighed microspheres were carefully poured though the funnel onto the graph paper until the apex of the conical pile just touches the bottom tip of the funnel. The radius(r) of the base of the conical pile was measured by drawing a circle around the pile. The angle of repose (θ) was calculated by using the following formula.

$\theta = \text{Tan}^{-1}h/r$

Where, θ is Angle of repose

h is height in cm

r is radius

F) Partical size: The particle size of prepared mucoadhsive microspheres was measured by microscopic technique by using standard electron microscope for about 100 particles were measured and their average size was determined. The mucoadhsive microspheres and settled portions of microspheres were recovered separately and were dired and weighed.

Invitro wash off test: The mucoadhesive properties of the microspheres were evaluated by the invitro wash off test. A2 X 3 cm piece of goat intestine mucosa was tied on to a glass slide using thread. Microspheres were spread (~50) onto the wet, rinsed, tissue specimen and the prepared slide was hung onto to the one of the grooves of the USP tablet dissintegrating test apparatus.

The dissintegrating test apparatus was operated such that the tissue specimen was given regular up and down movements in the beaker containing the simulated gastric fluid USP pH 1.2 buffer. At the end of 30 minutes, 1 hr and at hourly intervals up to 8 hrs the number of microspheres still adhering onto the tissue was counted. The results of invitro wash off test of batches B1 to B7 were shown in table no 5 and 6.

RESULTS AND DISCUSSION

The results concluded that the micrometric studies of mucoadhesive microspheres have concluded that, the micrometrics found to be shown in table no 3 and 4 excellent flow properties, where as invitro comparision studies found to be shown that batches B5, B6 and B7 have shown good mucoadhesion properties in table no 5.

Table 3: Flow properties of all formulations

BATCH CODE	ANGLE OF REPOSE (θ)	BULK DENSITY (g/cm2)	TAPPED DENSITY (g/cm2)	HAUSNERS RATIO	CARRS INDEX
B1	15	0.61	0.68	1.09	10.29
B2	11	0.80	0.87	1.09	8.04
B3	13	0.70	0.76	1.08	7.89
B4	19	0.51	0.56	1.09	8.92
B5	12	0.79	0.85	1.07	7.05
B6	14	0.68	0.81	1.19	16.04
B7	16	0.71	0.81	1.14	12.34

Table 4: Mean particle size of all formulations.

BATCH CODE	PARTICLE SIZE µm
B1	124.35
B2	112.70
B3	109.78
B4	154.64
B5	110,9
B6	119.88
B7	140.48

Table 5: percent mucoadhesive property of all formulations in pH 1.2 buffer

Time (hr)	B1	B2	B3	B4	B5	B6	B7
0.5	45%	80%	55%	59%	92%	87%	88%
1	30%	75%	37%	40%	88%	81%	88%
2	10%	63%	15%	17%	88%	79%	88%
3	---	50%	---	---	82%	79%	81%
4	---	40%	---	---	82%	79%	81%
5	---	35%	---	---	82%	79%	81%
6	---	27%	---	---	82%	75%	78%
7	---	15%	---	---	80%	70%	75%
8	---	10%	---	---	78%	65%	70%

CONCLUSION

The mucoadhesive microspheres using different polymers were sucessfully formulated by ionotropic gelation method. All the formulations have shown good flow properties and good particle size. The invitro wash off comparision test were carried out in 1.2 pH buffers and B5 Batch has shown good results in all aspects.

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