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Short Communiucation

EFFECT OF GLUTERALDEHYDE AS A CROSS LINKING AGENT IN THE PREAPARTION OF ALGINATE MICROSPHERES

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Abstract

Background: *Microspheres are commonly free-flowing powders possessing a particle size ranging from 1-1000 µm comprising of synthetic polymers or proteins. Microspheres are multi-particulate drug delivery systems which are prepared to obtain prolonged or controlled drug delivery to improve bioavailability, stability and to target the drug to a specific site at a predetermined rate.* ***Objectives:*** *The aim of this study is to formulate and evaluate alginate microspheres and their effect on glutaraldehyde as a cross-linking agent incorporating Metformin Hydrochloride as a model drug.* ***Methods****: Different formulations of alginate microspheres are prepared, the one using glutaraldehyde as a crosslinking agent and the other one is without, so the effects of glutaraldehyde can be measured by performing different evaluation parameters like IR, particle size, micromeritic properties, drug content, drug loading, drug entrapment efficacy. The in vitro drug release activity is carried out of both the formulations.* ***Results and Discussion:*** *The in vitro drug release data of different formulations was studied in three different pH media (pH 1.2 for 2 hours, pH 6.8 for 5 hours and pH 7.4 for 3 hours). After carrying out the experiment at pH 1.2, a slight drug release has been observed for both the formulations. However, a change in pH 1.2 to 6.8 increased the drug release, the formulation containing without glutaraldehyde shows maximum drug release compared to formulations with glutaraldehyde. At pH 7.4 the formulation with glutaraldehyde shows a steady-state drug release.* ***Conclusion:*** *In our study, it was found that gluteraldehyde concentration changed the drug release properties of prepared microspheres and hence can be used as an effective cross linking agent to achieve a controlled release formulation after further studies.*

Keywords: Cross-linking agent; Alginate Microspheres; Glutaraldehyde; Drug release

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Introduction

Microspheres belong to multiparticulate drug delivery systems which are basically adapted to obtain controlled or prolonged drug delivery to enhance stability, bioavailability and to target the drug to a specific site at a predetermined rate. They are obtained from protective or polymeric waxy materials such as natural, semi synthetic and synthetic polymers. Microspheres are obtained from synthetic polymers or proteins, commonly free flowing powders which possesses a particle size ranging from 1-1000 μm. The technique for the preparation of microspheres offers more than one alternative to govern as drug administration factors and to enhance the therapeutic efficacy of a given drug [1]. In contrast to conventional dosage forms these delivery systems provide various advantages that includes, patient compliance and convenience, reduced toxicity with improved efficacy. Microsphere can be prepared by diverse types of material such as polymers, glass, and ceramic microspheres [2]. The microspheres processed by thermal cross-linking and glutaraldehyde displayed good stability in HCl as compared with microspheres prepared by emulsification ionotropic gelation and tripolyphosphate [3].

Materials and Methods

All chemicals and reagents were procured commercially from HiMedia Lab. Pvt. Ltd. (Germany) and Merck Specialists Pvt. Ltd. (Germany). Infrared (IR) spectra were obtained on a Bruker Alpha Fourier Transform (FT-IR) spectrophotometer and are reported in terms of frequency of absorption (υ, cm-1). Dissolution study was performed on a dissolution apparatus, Labindia.

Preparation of alginate microspheres

The required amount of sodium alginate was taken in a beaker and mixed it nicely till it gets dissolved properly (Solution 1). After getting completely dissolved, required amount of metformin hydrochloride was added in the above mixture (Solution 1), whereas in another beaker required amount of calcium chloride was taken and mixed it thoroughly (Solution 2). Solution 1 was added drop-wise to the mixture of solution 2 with the help of syringe (24 gauge) while the magnetic stirrer was in running condition. After adding the solution successfully keeps the magnetic stirrer on for 2 hrs. The prepared microspheres were filtered out and were added in the mixture of glutaraldehyde (25%) solution. The solution was placed for 30 min. The microsphere were filtered and washed out with ethanol. The prepared

microspheres were placed in the petri dish and kept it to dry in an oven at 50^{o}C for 24 hrs. Similarly, another formulation of alginate microspheres was prepared without using glutaralaldehyde, both the formulation are evaluated and the effect of glutaraldehyde their release properties were measured.

Results and Discussion

In vitro dissolution studies of alginate microspheres was performed using USP II dissolution apparatus at 50 rpm at 37 ± 0.5°C in the 900 ml of gastric fluid pH 1.2 for 2 hours followed by 900 ml of intestinal fluid pH 6.8 and pH 7.4 for 8 hours. The release properties containing gluteraldehyde show a steady state drug release as compared to the formulation without gluteraldehyde.

Table 1: Results of *in vitro* drug release study (with Glutaraldehyde)

Time (min)	Absorbance	Conc. (µg/ml)	Amount in 10 ml (mg)	Amount in 900 ml (mg)	Loss (mg)	Cummalative Loss (mg)	CDR	% CDR
0	0	0	0	0	0	0	0	0
15 min	0.022	0.104	0.0001	0.093	0	0	0.093	3
30 min	0.035	0.250	0.0002	0.223	0.0001	0.0001	0.2231	7.12
1 hr	0.041	0.391	0.0004	0.351	0.0002	0.0004	0.3510	11.23
2 hr	0.057	0.670	0.0007	0.602	0.0004	0.0007	0.6027	19.24
3 hr	0.078	0.974	0.0010	0.876	0.0007	0.0014	0.8774	28.01
4 hr	0.102	1.330	0.0013	1.197	0.0010	0.0024	1.1993	38.25
5 hr	0.138	1.720	0.0017	1.544	0.0013	0.0036	1.5476	49.33
6 hr	0.161	2.333	0.0023	2.101	0.0017	0.0053	2.106	67.11
7 hr	0.193	2.686	0.0027	2.42	0.0023	0.0076	2.4276	77.25
10 hr	0.216	3.014	0.0030	2.704	0.0027	0.0102	2.7142	86.93

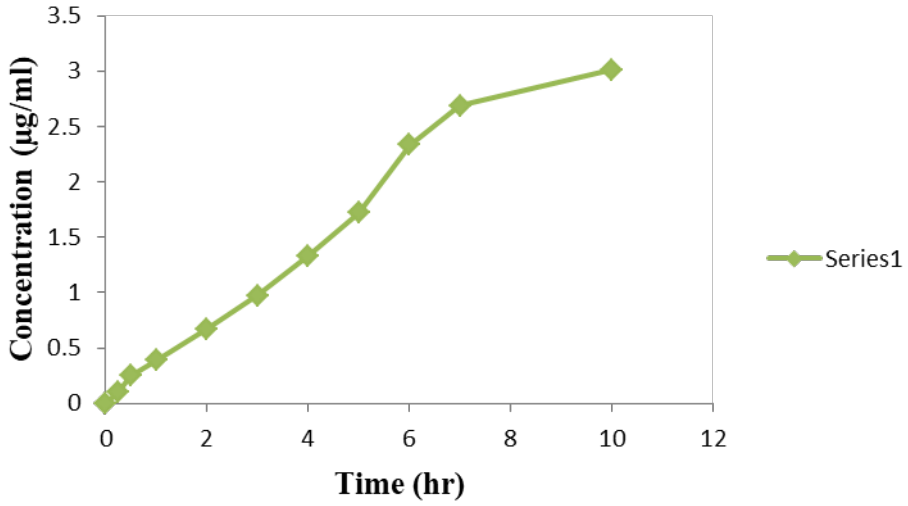

Figure 1: *In vitro* drug release profile of prepared microspheres (With glutaraldehyde)

Table 2: Results of *in vitro* drug release data (Without Glutaraldehyde)

Time (min)	Absorbance	Conc. (µg/ml)	Amount in 10 ml (mg)	Amount in 900 ml (mg)	Loss (mg)	Cummalative loss (mg)	CDR	% CDR
0	0	0	0	0	0	0	0	0
15 min	0.029	0.109	0.0002	0.121	0	0	0.1841	7
30 min	0.044	0.261	0.0004	0.245	0.0002	0.0002	0.2561	11.23
1 hr	0.048	0.407	0.0006	0.387	0.0004	0.0007	0.3871	15.41
2 hr	0.065	0.696	0.0009	0.713	0.0006	0.0011	0.6249	24.20
3 hr	0.099	0.982	0.0012	0.917	0.0009	0.0023	0.9856	42.10
4 hr	0.156	1.356	0.0017	1.225	0.0012	0.0025	1.2154	45.24
5 hr	0.207	2.546	0.0045	2.224	0.0017	0.0058	2.1760	72.45
6 hr	0.623	3.476	0.0068	2.704	0.0045	0.0127	2.9411	89.51

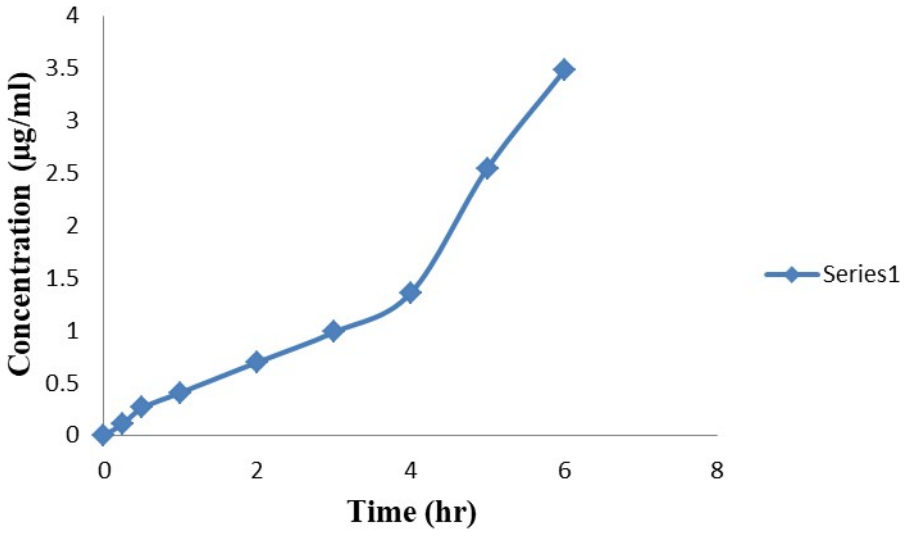

Figure 2: *In vitro* drug release profile of prepared microspheres (Without glutaraldehyde)

Conclusion

The results obtained from *in vitro* data revealed that the prepared metformin hydrochloride microspheres crosslinked with glutaraldehyde were having good buoyancy and better drug release than crosslinked without glutaraldehyde. The addition of crosslinking agent with glutaraldehyde produces more appropriate controlled release formulation. As glutaraldehyde is an added % release of drug is decreased. So, it can be concluded that microspheres of Metformin hydrochloride drug prepared with crosslinking agent glutaraldehyde provide a convenient dosage form for achieving better floatation and drug release.

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