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Synthesis and evaluation of pH dependent hydrogels for controlled release of venlafaxine HCl

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SUMMARY

pH dependent hydrogel formulations of venlafexine HCl were prepared by free radical polymerization method using polyethylene glycol as polymer. Various samples were prepared with varying concentration of polymer, monomer and cross-linker to study their effect on gel swelling, diffusion characteristics and drug release. Swelling was found to be increased with increase in pH. Increase in acrylic acid concentration increases swelling while increase in cross-linker concentration has an opposite effect on swelling. Drug release study was performed in pH 1.2, 5.5 and 7.5 for 12 hours at 37 °C and drug release was found to increase in higher pH. Prepared hydrogel preparations were also characterized by PXRD, TGA, SEM and FTIR.

INTRODUCTION

Hydrogels are three dimensional hydrophilic polymeric networks intended to swell in water and maintain their structure while holding a large amount of water. Over the past few decades, hydrogels have successfully been used as a drug delivery system for controlled release of active agent (Ahmed, 2015). Effective functioning of a hydrogel is dependent on the composition of the formulation which includes polymer and cross linkers. Most commonly studied ionic polymers for pH-responsive behaviour include poly acrylic acid (PAA), polyethylene glycol (PEG), polyvinyl alcohol (PVA), polyacrylamide (PAAm), and polypeptides. PEG based hydrogels have wide applications in medicine because they are non-toxic and (Alconcel et al., 2011). Physical properties such as water permeability and mechanical strength of PEG hydrogels can be easily controlled purposefully by changing the molecular weight of PEG (Lee et al., 2007).

In this study attempts have been made to prepare a PEG based pH dependent hydrogel formulation of an anti-depressant agent called venlafaxine HCl. Short half-life and high daily dosing (75-450 mg) of the drug requires frequent dosing which may result in low patient compliance. It also shows abrupt release in the stomach and causes nausea, dizziness and GI irritation. Therefore the aim of this study was to prepare a controlled release formulation to avoid frequent administration of the drug with low adverse effects.

MATERIALS AND METHODS

Venlafaxine HCl was received as a kind gift from Glitz Pharmaceuticals Islamabad. Acrylic Acid, Polyethylene glycol, N, N′- methylene bisacryl amide and Benzyl peroxide were received from Sigma Aldrich.

Free radical polymerization method was employed for the preparation of hydrogels using acrylic acid

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and PEG. Nine different formulations were prepared with varying concentrations of polymer, monomer and cross-linker. Prepared hydrogel formulations were evaluated for swelling parameters, drug loading and diffusion coefficient. Physicochemical characterization was performed by PXRD, FTIR, SEM and TGA. In vitro release studies were performed by using USP-II apparatus in three buffer solutions (0.05 M) of pH 1.2, 5.5 & 7.5.

RESULTS AND DISCUSSION

Table 1 shows degree of swelling of the hydrogels in phosphate buffer (0.05 M) solutions of different pH values. Both dynamic and equilibrium swelling coefficient were increased with pH and maximum swelling was observed at 7.5 pH. Higher pH resulted in more swelling of the gel. As expected, these results can be attributed to the increase in the degree of interaction between the PEG and AA due to ionization of carboxyl groups at higher pH i.e. greater than the pK_a of the gel.

Fig 1 shows SEM pictures of prepared hydrogel. Samples without drug show relatively smooth and homogenous morphology while drug loaded micrographs show rough surfaces and aggregation in morphology due to drug incorporation. Dispersed white particles of drug can be seen throughout the hydrogel network.

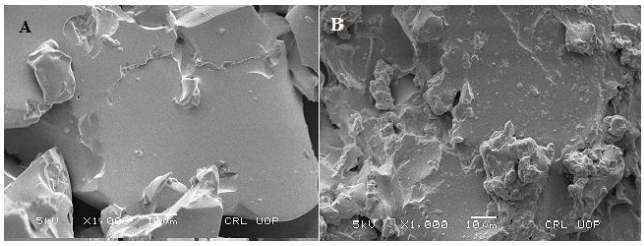

Fig. 1. *SEM micrographs of AA/PEG hydrogels without drug (A) and drug loaded (B) at magnification (x1000).*

Fig 2 shows a representative release profile of drug from a hydrogel formulation. All the formulations have shown similar type of profile, where higher pH of dissolution medium results in better and more controlled release of drug. FTIR, PXRD and TGA results have shown better interaction among the component of hydrogel formulation.

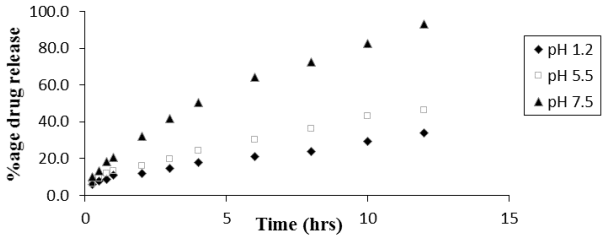

Fig. 2. *Percentage release of drug from AA/PEG hydrogel (22/4) having MBA concentration (0.75 % of AA) (D1)*

CONCLUSIONS

A PEG based pH dependent hydrogel formulation of Venlafaxine HCl was successfully prepared. The dissolution profile of the drug from hydrogel demonstrates release over an extended period.

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Table1. Dynamic & equilibrium swelling coefficients of hydrogels at different pH.

Sample ID	Dynamic swelling co-efficient				Equilibrium swelling co-efficient			
	pH 1.2	pH 5.5	pH 6.5	pH 7.5	pH 1.2	pH 5.5	pH 6.5	pH 7.5
B_1 (10/4)	1.38	1.43	2.40	2.96	1.75	2.27	9.05	13.87
B_2 (16/4)	1.51	1.63	2.53	3.01	1.98	2.60	9.55	14.24
B_3 (36/4)	1.73	1.82	2.68	3.16	2.18	2.85	10.08	14.74
C_1 (22/4)	1.47	1.48	2.20	2.78	1.89	2.20	8.00	14.21
C_2 (22/6)	1.58	1.64	2.22	3.07	2.04	2.22	8.19	14.89
C_3 (22/8)	1.69	1.86	2.25	3.21	2.22	2.38	8.53	15.14
D_1 (22/4)	1.57	1.62	2.30	3.03	1.95	2.38	9.13	16.06
D_2 (22/4)	1.38	1.49	2.17	2.78	1.76	2.15	7.72	13.23
D_3 (22/4)	1.33	1.42	2.02	2.63	1.67	1.93	6.55	11.28