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Development and Evaluation of Interpenetrating Polymer Network Hydrogel for Controlled Release of Cefadroxil

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Abstract

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs through pharmaceutical products of different dosage form. By increasing the concentration of cross linking agent drug entrapment efficiency increase but in case of percentage yield firstly it increases (A9-A10) after that in it decrease. Out of all the 12 formulations, A-10 formulation is optimized and taken for further characterization.

Keywords: Cefadroxil, Controlled release, Hydrogel

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Introduction

Oral route is considered most natural, convenient and safe due to its ease of administration, patient acceptance, and cost-effective manufacturing process. Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. Conventional drug delivery suffer from certain drawbacks like increased fluctuation in the circulatory drug level, more frequency of dosage administration, increased G.I. irritation and dose related side effects. To overcome these disadvantages, control release oral drug delivery systems were designed. In the past few decades, the ways of administering drugs have gained increasing attention. Development of administration methods that allow the patients to safely treat themselves is as important as any other health care development. Oral route of drug delivery has been the most convenient and commonly employed route of drug delivery. The oral route is preferred due to its convenience, low cost and better patient compliance. Conventional drug delivery suffer from certain drawbacks like increased fluctuation in the circulatory drug level, more frequency of dosage administration, increased G.I. irritation and dose related side effects. To overcome these disadvantages, controlled release oral drug delivery systems were designed.[1,2] Controlled release drug delivery systems are designed for uniform and constant drug release over a prolonged period of time. The constant drug release is achieved by use of various polymeric systems which act as rate controlling membrane for the release of drug. It was anticipated that developed formulations will offer following advantages:- 1. Whenever an IPN hydrogel is formed from two polymers at a given temperature, the physical phase separation between the component polymers would be almost impossible because of completely cross linking of polymers.

IPN is also attractive in producing synergistic properties from component polymers. For example, when hydrophilic gelling polymer is interpenetrated with a relatively hydrophobic gelling polymer, the resultant IPN hydrogel is expected to have an improved capability of immobilizing a drug.

IPN enhance the mechanical properties of the final product.

Thermodynamic incompatibility can be overcome due to permanent interlocking of the network segments preformulation studies.

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a) Melting point.
b) Solubility.
c) Partition coefficient.
d) Ultra-violet Spectroscopy (standard calibration curve of pure drug).
e) Fourier transform infrared spectroscopy.
f) High performance liquid chromatography.

2. Development of Interpenetrating polymer network hydrogel containing drug (Cefadroxil) 3. Optimization and Evaluation studies of prepared interpenetrating polymer network hydrogel a) Percentage (%) yield b) Drug Entrapment efficiency c) Swelling studies d) Scanning electron microscopy e) Fourier transform infrared spectroscopy f) X-ray Diffraction g) *In vitro* release studies h) *In vitro* release kinetics 4. Stability studies of prepared interpenetrating polymer network hydrogel.[3]

Materials and Methods

Cefadroxil was obtained from Hetero Labs. Ltd., Baddi, India. All the excipients used were of analytical grade.

Methodology and Results

Optimization of Amount of Polymer

To optimize the amount of polymer, different formulations (A-1, A-2, A-3, A-4, A-5, and A-6) were prepared. The result

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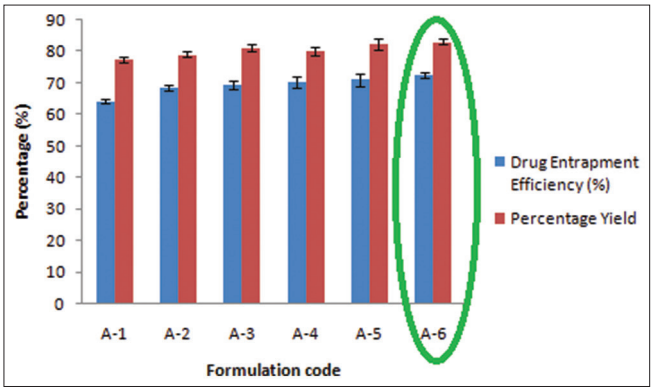

Figure 1: Percentage (Drug entrapment efficiency and Percentage Yield) versus formulation code graph of IPN Hydrogel formulations (A-1 to A-6)

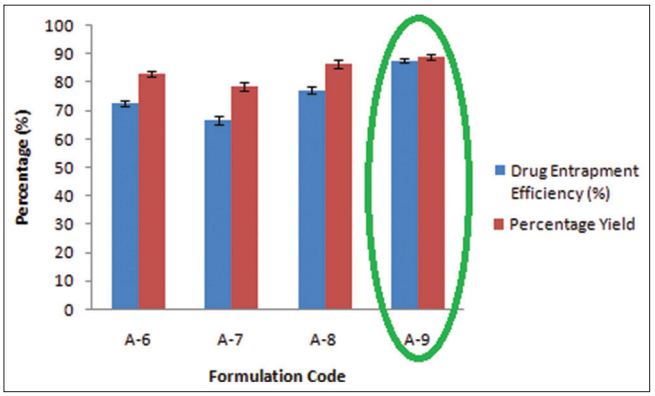

Figure 2: Percentage (Drug entrapment efficiency and Percentage Yield) versus formulation code graph of IPN Hydrogel formulations (A-6 to A-9)

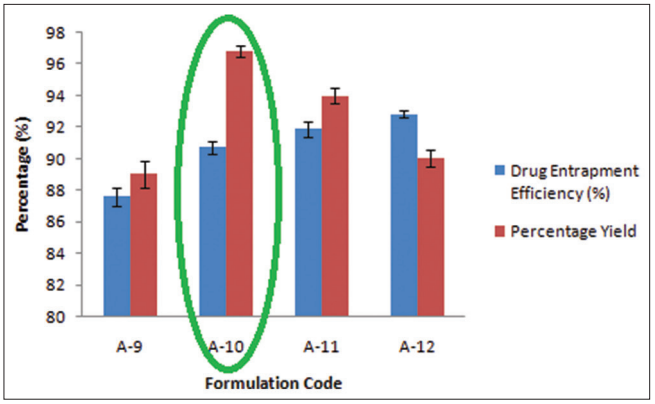

Figure 3: Percentage (Drug entrapment efficiency and Percentage Yield) versus formulation code graph of IPN Hydrogel formulations (A-9 to A-12)

obtained were tabulated and graphically represented. In A-1, A-2 and A-3, concentration of chitosan was changed while concentration of PVP was kept constant. In formulation A-1, A-2 and A-3 when concentration of chitosan was increased increase in drug entrapment efficiency, percentage yield and percentage cumulative drug release is shown [Figures 1-5].

In formulation (A-4, A-5 and A-6) with decrease in PVP concentration the drug entrapment efficiency, percentage yield

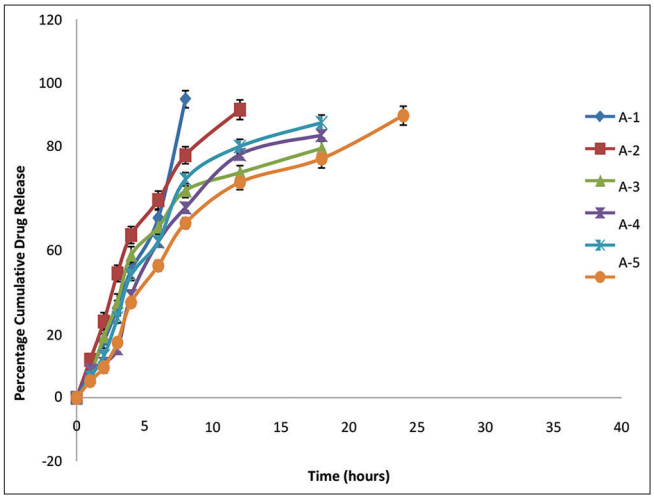

Figure 4: Percentage cumulative release versus time graph of IPN Hydrogel formulations (A-1 to A-6)

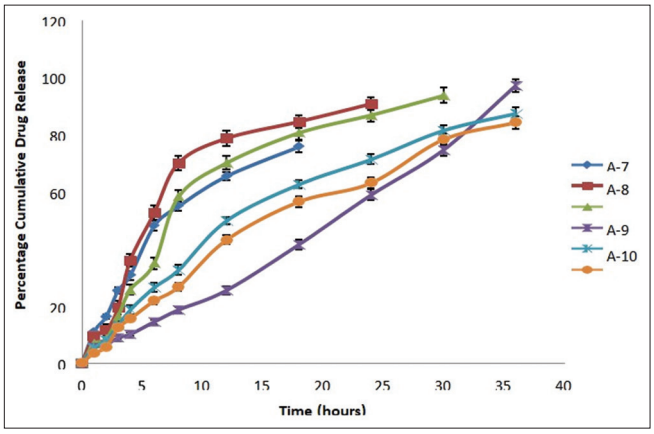

Figure 5: Percentage cumulative drug release

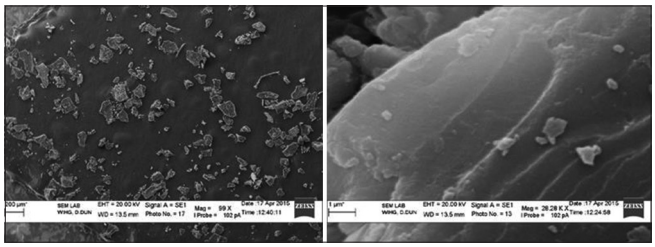

Figure 6: SEM images of unswellon IPN hydrogel

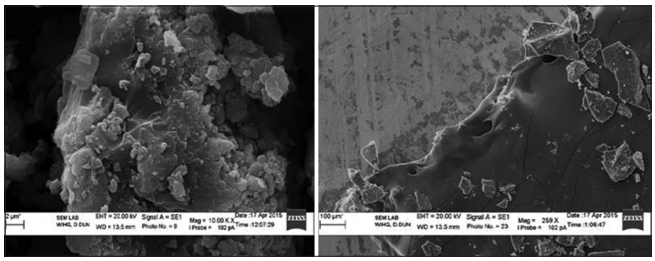

Figure 7: SEM images of swellon IPN hydrogel

and percentage cumulative drug release increase. From all the above, we conclude that as the concentration of chitosan increase

drug entrapment efficiency, percentage yield and percentage cumulative drug release increase but in other hand decrease in concentration of PVP leads to increase in drug entrapment efficiency, percentage yield and percentage cumulative drug release in formulation A-1 to A-6.

Table 1 : Result of optimization of amount of polymer

Formulation code	*Drug entrapment efficiency (%) (±S.D)*	*Percentage yield (%) (±S.D)*	*Percentage cumulative drug release in time (±S.D)*
A-1	64.142±0.64	77.276±0.92	94.78±1.96 in 8 h
A-2	68.527±0.95	79.023±0.85	91.432±1.99 in 12 h
A-3	69.372±1.43	81.218±0.93	79.107±1.94 in 18 h
A-4	70.381±1.69	80.012±1.42	83.29±1.88 in 18 h
A-5	71.050±1.92	82.245±1.66	87.294±1.95 in 18 h
A-6	**72.520±0.91**	**83.047±0.90**	**89.538±1.98 in 24 h**

Table 2: Result of optimization of amount of drug

Formulation code	*Drug entrapment efficiency (%) (±S.D)*	*Percentage yield (%) (±S.D)*	*Percentage cumulative drug release in time*
A-6	72.520±0.91	83.047±0.90	89.538±1.98 in 24 h
A-7	66.726±1.42	78.54±1.42	75.542±1.90 in 18 h
A-8	77.247±1.15	86.528±1.26	90.518±1.93 in 24 h
A-9	**87.613±0.73**	**89.013±0.82**	**93.435±1.94 in 30 h**

Table 3: Result of optimization of amount of cross linking agent

Formulation code	*Drug entrapment efficiency (%) (±S.D)*	*Percentage yield (%) (±S.D)*	*Percentage cumulative drug release in time*
A-9	87.613±0.58	89.013±0.82	93.435±1.94 in 30 h
A-10	**90.710±0.37**	**96.805±0.36**	**96.78±1.89 in 36 h**
A-11	91.896±0.48	94.011±0.49	87.238±1.81 in 36 h
A-12	92.812±0.22	90.054±0.51	84.0424±1.88 in 36 h

Optimization of Amount of Drug

Amount of drug was optimized by formulating different formulation (A-6, A-7, A-8 and A-9) by changing quantity of drug (150, 100, 200, and 250 mg) and other parameters (polymer concentration, cross linking agent) were kept constant in each formulation.

We can see that as the concentration of drug decrease drug entrapment efficiency, percentage yield and percentage cumulative drug release also decrease as shown in formulation A-7 but further increase in drug quantity lead to increase in drug entrapment efficiency, percentage yield and percentage cumulative drug release. From all this, we can observe as the concentration of drug increases it leads to increase in drug entrapment efficiency, percentage yield and percentage cumulative drug release. We can conclude that A-9 formulation contains highest drug entrapment efficiency, percentage yield and percentage cumulative drug release so this is optimized amount of drug (250 mg) which we used in preparation of optimized formulation [Tables 1-3].[4-6]

In Vitro Drug Release Studies

In vitro drug release study was carried out for all the formulation in phosphate buffer of pH 7.4 using dissolution apparatus (paddles type). Out of all the formulation A-10 formulation give us prolonged drug release (36 h) with good drug entrapment efficiency increase (90.710 ± 0.37), percentage yield (96.805 ± 0.36) and percentage cumulative drug release (96.78 ± 1.89). So A-10 is the optimized formulation. We also discuss the Effect of Polymer ratio, Effect of Drug Content and Effect of Cross linking Agent on percentage cumulative drug release below [Tables 4 and 5].[7-10]

Scanning Electron Microscopy

Surface morphology of interpenetrating polymer network hydrogel was examined by Scanning electron microscopy. Scanning electron

Table 4: Percentage cumulative drug release with standard deviation of formulations i.e., A-1, A-2, A-3, A-4, A-5 and A-6

Time (hrs)	*A-1*	*A-2*	*A-3*	*A-4*	*A-5*	*A-6*
0	0	0	0	0	0	0
1	8.131±2.21	12.033±2.0	7.231±2.23	8.908±0.22	6.567±1.41	5.275±1.62
2	18.01±2.32	24.231±2.83	19.326±2.40	10.991±0.43	13.215±1.54	9.622±1.85
3	28.46±2.42	9.455±2.64	30.338±2.61	15.512±0.61	25.337±1.67	17.535±1.13
4	40.45±2.54	51.64±2.71	45.157±2.83	32.395±1.81	38.981±1.89	30.234±1.56
6	57.07±2.63	62.74±2.97	54.092±2.12	49.523±1.17	49.592±1.74	41.899±1.74
8	94.78±2.71	77.01±2.69	65.725±2.27	60.318±1.29	69.329±2.13	55.414±1.69
12	-	91.43±3.12	71.381±2.34	77.226±1.42	79.784±2.23	68.353±2.32
18	-	-	79.107±2.46	83.29±1.68	87.29±2.42	75.867±2.95
24	-	-	-	-	-	89.538±3.0
30	-	-	-	-	-	-
36	-	-	-	-	-	-

Table 5: Percentage cumulative drug release with standard deviation of formulations i.e., A-7, A-8, A-9, A-10, A-11 and A-12

Time (hrs)	*A-7*	*A-8*	*A-9*	*A-10*	*A-11*	*A-12*
0	0	0	0	0	0	0
1	10.895±0.67	9.254±1.92	6.702±1.23	5.433±0.32	5.212±0.42	3.442±0.22
2	16.134±0.89	11.327±2.12	8.326±1.42	6.411±0.37	7.931±0.65	5.541±0.35
3	25.265±1.0	19.375±2.31	16.318±1.67	8.788±0.48	13.043±1.23	12.309±0.63
4	30.538±1.54	35.816±2.21	25.591±1.86	10.003±0.56	18.527±1.52	15.371±0.98
6	47.916±1.72	52.518±2.41	34.764±2.14	14.338±0.83	26.395±1.64	21.722±1.29
8	54.724±1.69	69.836±2.52	58.04±2.29	18.521±0.99	32.409±1.69	26.485±1.45
12	65.259±1.32	78.452±2.63	69.889±2.31	25.348±1.43	49.723±1.32	42.99±1.61
18	75.542±1.95	84.275±2.12	80.387±2.45	41.289±1.65	62.401±1.55	56.326±1.79
24	-	90.518±2.26	86.628±2.52	58.629±1.87	71.192±1.73	62.907±1.96
30	-	-	93.435±2.65	74.325±1.98.	81.281±1.89	78.106±2.06
36	-	-	-	96.78±2.22	87.238±1.92	84.0424±2.24

microscopy was carried out to study surface morphology, shape, texture, and porosity of hydrogel. It was observed that hydrogel are irregular in shape and surface of unswellon hydrogel was smooth show no surface pores [Figures 6 and 7].[11]

Results and Conclusion

Cefadroxil is a first generation cephalosporin antibacterial drug that is Para-hydroxyl derivative of cefalaxin and used for the treatment of Urinary tract infection, skin and skin structure infection pharyngitis and/or tonsillitis similarly in treatment of mild-to-moderate susceptible infections. Cefadroxil binds to specific penicillin-binding proteins located inside the bacterial cell wall, and inhibits bacterial cell wall synthesis, which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis. Bacteria eventually lyse due to ongoing activity of cell wall autolysis enzymes (autolysins and murein).

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