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FORMULATION AND EVALUATION OF DICLOFENAC SODIUM GELS WITH DIFFERENT POLYMERS

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ABSTRACT

This study aims to prepare and evaluate Diclofenac sodium gels with different polymers. In this different polymers carbopol1934 P,HPMC K 100,pemulen TR-1,pemulen TR-2,lutrol F 127,xanthan gum with different concentrations are used. They were evaluated for physicochemical properties such as physical appearence pH, spreadability, viscosity, extrudability and drug content.

KEYWORDS: semi solid dosage form, gels, diclofenac sodium, drug content.

BASIC INTRODUCTION

Semi solid pharmaceutical system comprises a body of product, which when applied to skin or accessible mucous membranes tend to alleviate or treat a pathological condition or other protection against harmful environment.

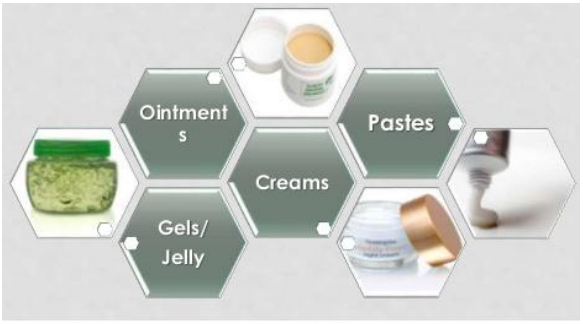


Fig. 1: Semi solid dosage forms.

Fig. No 2 gel

GELS

- Gels are semisolid system in which liquid phase is constrained with a 3-D polymeric matrix having a high degree of physical or chemical crossing
- Gels are aqueous colloidal system of hydrated forms of insoluble medicaments
- Gels are transparent or translucent non greasy semisolid and contain water

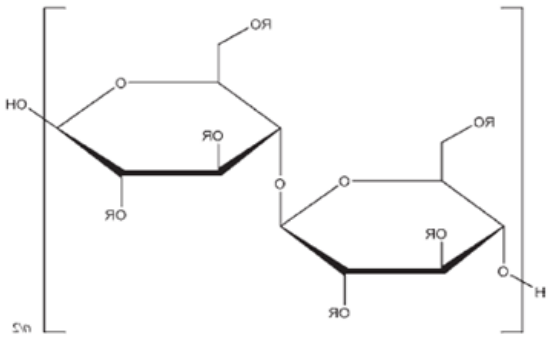
Uses

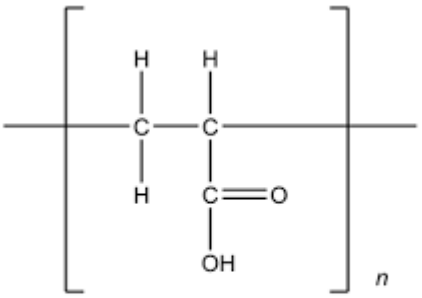
- Drug delivery mediums for topical and oral pharmaceuticals
- organic application mediums for cosmetics
- cleaning materials for art conservation
- as delivery mediums and/or nutrients in nutraceuticals (vitamins and supplements),
- Particles in personal care products (shampoo, conditioner, soap, toothpaste, etc.)
- A crystalline fat alternative in food processing.

MATERIALS AND METHODS

1) HPMC K 100

Synonym : Hypromellose.
Molecular Formula: $C_{56}H_{108}O_{30}$
Molecular Weight: 1261.45 g/mol.
Structure:





Acrylic acid monomer unit in carbomer polymers.

Category: Excipient, water retaining agent, thickening agent.

2) Carbapol 934 p:

Synonym: (1)-2-Methylbutyric acid

IUPAC name: 2 methyl butanoic acid.

Chemical formula: $C_5H_{10}O_2$

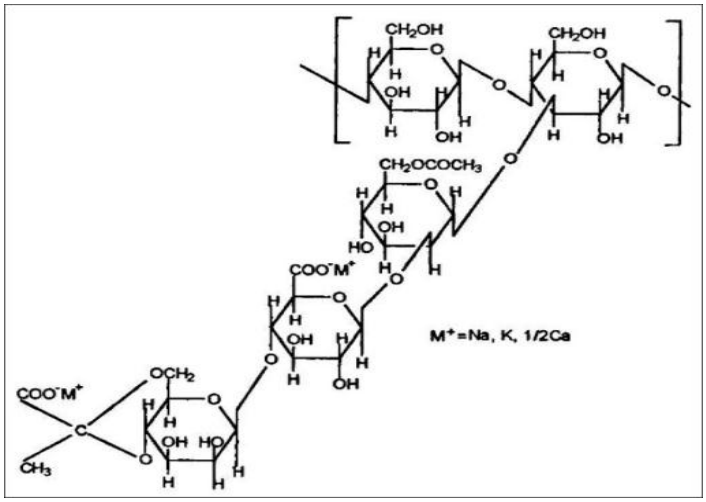
Structure

3) Xanthane gum

Synonyms: xantham; xanthan;keltrol f;rhodopol 23;glucomannan;gum xanthan;
Xanthan gum; xanthategum; xantempo(tm); xanthane gum

Molecular formula: $C_{35}H_{49}O_{29}$

Structure



METHOD OF PREPARATION

Preparation of Diclofenac sodium gel: 1 g of Diclofenac sodium was dissolved In weighed quantity of glycerin with the aid of mild heat (solution A).weighed quantity of polymer was added to 75 ml of distilled water and stirred until it dissolve (solution B).solution A and B were mixed thoroughly and final weight made up to 100 g.

Evaluation of Diclofenac sodium Gel Formulations

Prepared gels formulations were evaluated for

1) Physical appearance
2) pH
3) Extrudability
4) Spreadability
5) Viscosity, and
6) Drug content

***In vitro* Drug release studies**

Procedure

- Polymer was soaked in water over night.
- The gelling agent was then stirred on an overhead stirrer (Remi Motors) for uniform mixing.
- The exact quantity of prepared extract was then added to the gelling agent with stirring to obtain gel.
- Propyl paraben &methyl paraben were added as preservatives.
- The final p^H of gel was adjusted to 7-8 using 10% sodium hydroxide solution

Table 1: Formulations of Carbopol 934P based DS Gels.

INGREDIENTS	CF1	CF2	CF3
Diclofenac sodium	10%	10%	10%
Carbopol934P	1%	3%	5%
Propyl paraben	0.01%	0.3%	0.5%
Methyl paraben	0.01%	0.3%	0.5%
10%NaoH	Q.S	Q.S	Q.S
PemulenTR-1	-	-	2%
Water	Q.S	Q.S	Q.S

Table 2: Formulations of HPMC K 100 based DS Gels.

INGREDIENTS	HF1	HF2	HF3
Diclofenac sodium	10%	10%	10%
HPMC K 100	1%	3%	5%
Propyl paraben	0.01%	0.3%	0.5%
Methyl paraben	0.01%	0.3%	0.5%
Water	Q.S	Q.S	Q.S

Table 3: Formulations of Pemulen TR-1 based DS Gels.

INGREDIENTS	P1F1	P1F2	P1F3
Diclofenac sodium	10%	10%	10%
PemulenTR-1	1%	3%	5%
10%NaoH	Q.S	Q.S	Q.S
Propyl paraben	0.01%	0.3%	0.5%
Methyl paraben	0.01%	0.3%	0.5%
Water	Q.S	Q.S	Q.S

Table 4: Formulations of Pemulen TR-2 based DS Gels.

INGREDIENTS	P2F1	P2F2	P2F3
Diclofenac sodium	10%	10%	10%
Pemulen TR-2	1%	3%	5%
10%NaoH	Q.S	Q.S	Q.S
Methyl paraben	0.01%	0.3%	0.5%
Propyl paraben	0.01%	0.3%	0.5%
Water	Q.S	Q.S	Q.S

Table No.5 Formulations of Lutrol based DS Gels.

INGREDIENTS	LF1	LF2	LF3
Diclofenac sodium	10%	10%	10%
Lutrol F 127	5%	15%	30%
Propyl paraben	0.01%	0.3%	0.5%
Water	Q.S	Q.S	Q.S

Table 6: Formulations of Xanthan gum based DS Gel.

INGREDIENTS	XF1	XF2	XF3
Diclofenac sodium	10%	10%	10%
Xanthan gum	0.5%	3%	5%
Propyl paraben	0.01%	0.3%	0.5%
Water	Q.S	Q.S	Q.S

RESULTS AND DISCUSSIONS

Calibration Curve of DICLOFENAC SODIUM

Table 7: Calibration curve data.

S. No.	Concentration (mcg/ml)	Absorbance at 277.5nm
1	4.64	0.20465
2	9.28	0.38656
3	13.92	0.56009
4	18.56	0.72635
5	23.2	0.90894
6	27.84	1.10823

The linear equation was y =0.0406x +0.0129 concentration (mcg/ml). Different standard concentration and their peak area values at 277.5 nm were shown in the table. At all concentration levels standard deviation was low. Goodness of fit of regression equation was supported by correlation coefficient value (R^2 value) 0.9992 (for drug). Hence developed method can be used for routine analysis in pharmaceutical form for drug release studies.

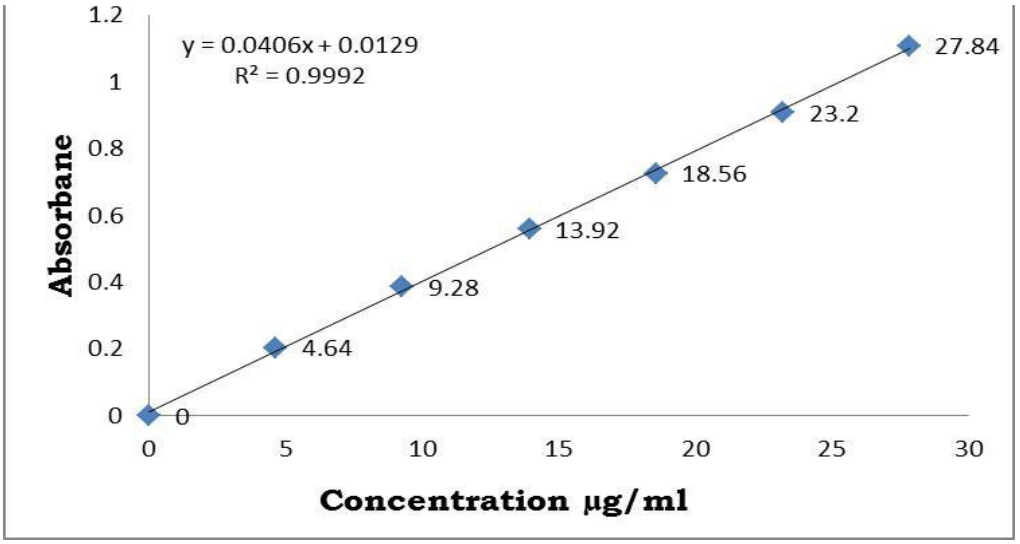


Fig. 3: Calibration curve.

Table 8: Evaluation of Physical Parameters of Prepared DS Formulations.

Formulation Code	Physical Appearance	Spreadability (gm/Sec)	Viscosity (Cps) X (X X 10^4)
CF1	White	4.60	6.555
CF2	White	4.40	6.333
HF1	White	4.95	5.397
HF2	White	4.55	5.397
P1F1	White	4.25	7.015
P1F2	White	3.26	7.111
P2F1	White	4.70	6.234
P2F2	White	3.24	6.012
LF1	White	5.15	4.702
LF2	White	3.15	4.702
XF1	White	5.50	6.576
XF2	White	4.50	5.787

Evaluation of physical parameters of prepared formulations

Table 9: Evaluation of physical parameters of prepared formulation.

FORMULATION CODE	pH	EXTRUDABILITY
CF1	3.5±0.011	Very poor
CF2	6.0±0.011	Poor
HF1	3.1±0.025	Poor
HF2	6.1±0.025	Poor
P1F1	3.8±0.027	Poor
P1F2	6.8±0.027	Poor
P2F1	3.1±0.033	Poor
P2F2	7.1±0.033	Poor
LF1	3.1±0.015	Very poor
LF2	4.1±0.015	Poor
XF1	3.9±0.024	Poor
XF2	5.9±0.024	Very poor

Evaluation of Physical Parameters of Optimized Formulations

Table 10: Evaluation of physical parameters of optimised formulations.

FORMULATION	APPEARANCE	SPREADABILITY (gm/sec)	VISCOSITY (Cps) x (X x 10^4)
CF3	White	1.57	1.555
HF3	White	1.62	2.397
P1F3	White	1.58	2.015
P2F3	White	1.59	3.012
LF3	White	1.58	2.702
XF3	White	1.60	4.175

Table 11: Evaluation of physical parameters of optimized formulations.

FORMULATION	pH	EXTRUDABILITY
CF3	5.5±0.011	Very good
HF3	5.1±0.025	Good
P1F3	4.8±0.027	Good
P2F3	4.1±0.033	Good
LF3	5.1±0.015	Very good
XF3	4.9±0.024	Good

Table 12: Percentage Cummulative Drug Release Profile of Optimized Formulations.

Time(hrs)	CF3	HF3	P1F3	P2F3	LF3	XF3
0.5	30.61 ±0.12	39.25 ±0.12	20.32 ±0.24	31.60 ±0.03	21.25 ±0.23	20.82 ±0.13
1	43.08 ±0.17	45.30 ±0.15	56.55±0.27	38.68 ±0.12	28.24 ±0.08	27.73 ±0.17
1.52	54.68 ±0.13	62.65 ±0.17	61.95 ±0.23	44.59 ±0.02	33.78 ±0.09	49.63 ±0.15
2.5	63.32 ±0.11	71.30± 0.18	74.92 ±0.22	50.28 ±0.03	49.99± 0.78	57.41 ±0.16
3	67.72 ±0.16	80.18± 0.10	86.09 ±0.21	57.20 ±0.05	63.18 ±0.06	72.76 ±0.05
4	76.00 ±0.18	89.33± 0.19	-	68.08 ±0.07	74.56 ±0.07	81.77 ±0.14
6	82.49 ±0.19	-	-	78.52 ±0.08	85.73 ±0.09	91.13 ±0.17
8	95.90 ±0.12	-	-	89.33 ±0.06	93.65± 0.08	-
% Assay	97.03	93.45	92.56	94.02	96.32	94.56

In vitro Diffusion Studies of Optimized Formulations

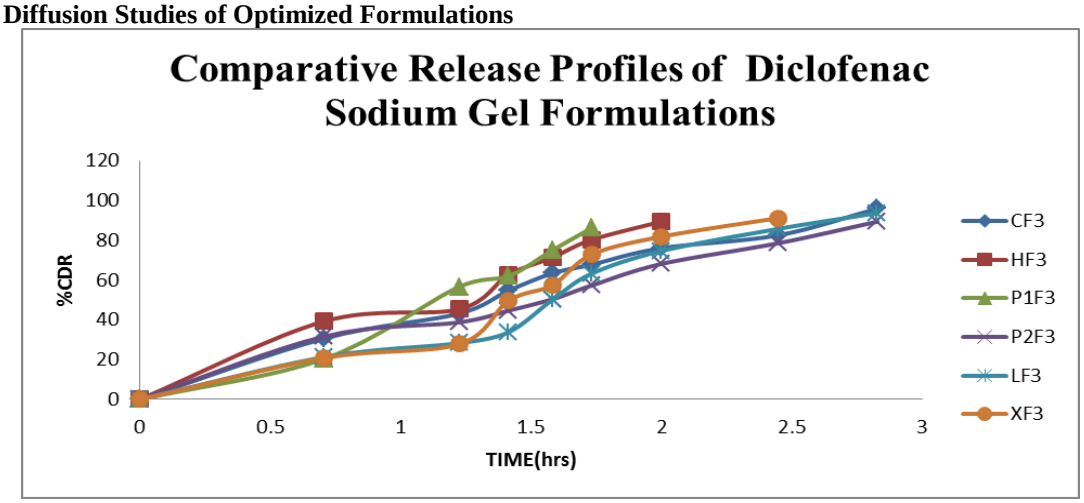


Fig. 4: Comparative release profile of DS gel formulation.

The order of drug release from matrix systems was described by using zero order or first order kinetics. The mechanism of drug release from matrix systems was studied by using higuchi equation and erosion equation and Peppas-Korsemeyer equation (Power Law) and the plots are give as.

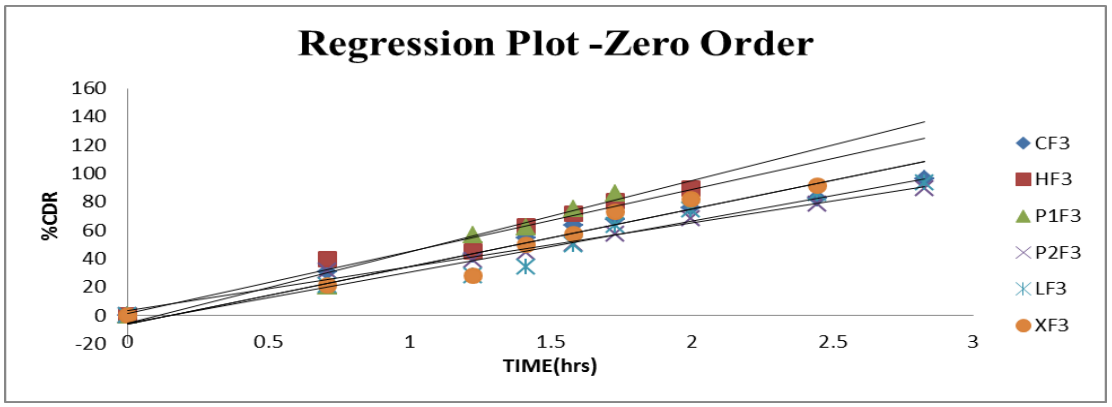


Fig. 5: Zero Order- Regression Plot of DS Gel Formulations.

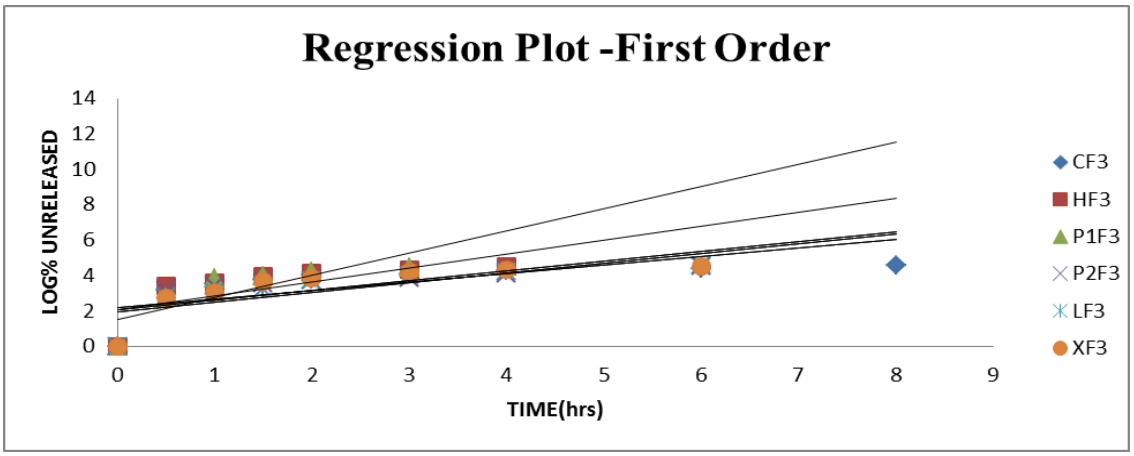


Fig. 6: First Order Regression Plot of DS Gel Formulations.

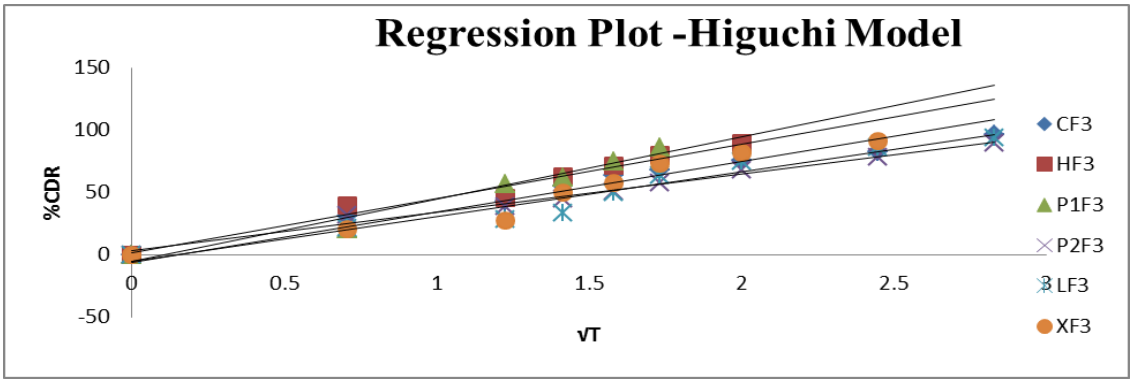


Fig. 7: Higuchi Model- Regression Plot of DS gel Formulations.

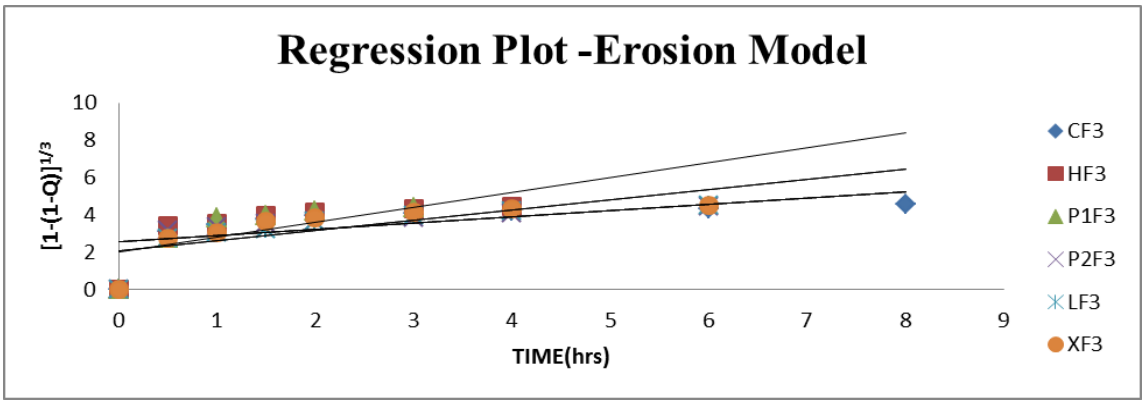


Fig. 8: Erosion Model -Regression Plot of DS Gel Formulations.

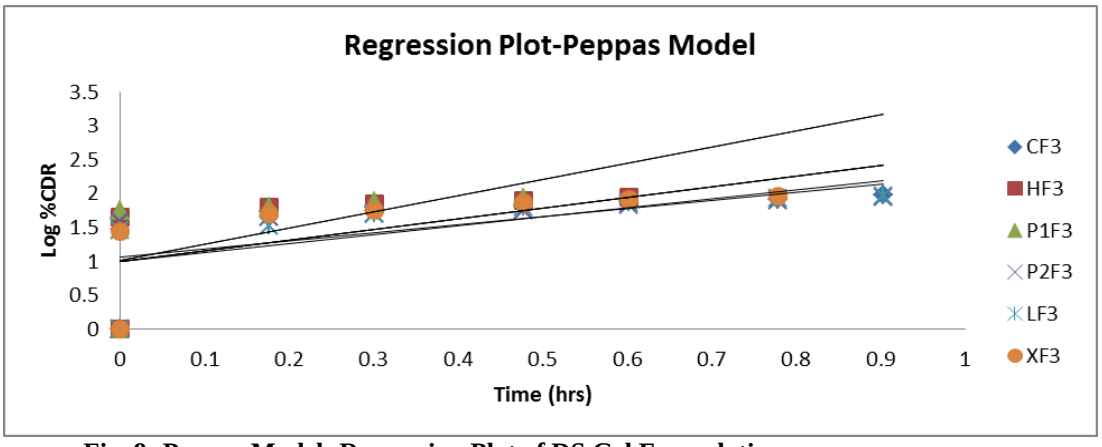


Fig. 9: Peppas Model -Regression Plot of DS Gel Formulations.

Table 13: Release Kinetics of optimized formulations.

GEL Formulation CODE	Zero order R^2 value	First order R^2 value	Higuchi R^2 value	Erosion R^2 value	Peppas 'n' value
C F3	0.996	0.778	0.978	0.413	0.712
HF3	0.985	0.835	0.972	0.515	0.549
P1F3	0.983	0.881	0.971	0.650	0.749
P2F3	0.980	0.847	0.986	0.482	0.718
LF3	0.996	0.889	0.950	0.599	0.647
XF3	0.995	0.871	0.941	0.556	0.538

CONCLUSION

All the DS Gel formulations were subjected to characterization of various physical parameters like Appearance, Spreadability, Viscosity, pH and Extrudibility as per the standard methods. pH values of various DS Gel formulations were found to be unsuitable, as the desired vaginal pH is between 4.5 and

5.5.

Owing to the inferior results of physical parameters, CF1,CF2, HF1, HF2, P1F1, P2F2, LF1, LF2, XF1 and XF2 Gel formulations of HS were not considered for further characterization.

By comparing the results of *in vitro* diffusion studies, DS Gel formulations consisting Carbopol 934P (CF3) was optimized due to its retarding ability and consistency. CF3 Gel formulation was subjected to further characterization.

By fitting the in vitro diffusion data into popular five regression and exponential models, all DS Gel formulations were found to be accepting zero order kinetics which was evident by higher R^2 values of zero order plot compared to R^2 values of first order plot that specifies independency of the concentration.

DS Gel formulations were found to be following Diffusion mechanism, which were evident by higher R^2 values of Higuchian plot compared to R^2 values of Erosion plot.

In order to assess the exact release mechanism, dissolution data of DS Gel formulations were fitted to Korsemeyer Pappas (Power Law) plot. All the exponent (n) values were found to be between 1.5 -1, which species that the Gel formulations were exhibiting Anomalous (Non-Fickian) transport mechanism for the drug release at rate controlled fashion.

No prominent difference was observed in the principal IR peaks of Pet. Ether extract of DS - Carbopol 934P optimized Gel formulations upon comparison with the peaks of DS gel and gelling agent alone, which may considered that DS gel and Carbopol 934P are compatible enough without any interactions.

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