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Formulation and evaluation of in-situ gels of hydrocartisone for the treatment of mouth ulcer

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Abstract
The present work was aimed to develop a in-situ gels and films of hydrocortisone for the treatment of aphthous ulcer. The in-situ gels and film was developed by using methylcellulose, based on the concept of temperature dependant gelling system. The sol-to-gel transformation occurred during the reduction of temperature. The in-situ gels were evaluated for gelling capacity, drug content, viscosity & in-vitro release were as in the film its evaluated for tensile strength, folding endurance, thickness etc. The experimental part shows that viscosity of the sol was increased by increasing the concentration of polymer. All the results were found to be satisfactory, when compared between the in-situ gels and films. The has shown the best formulation because of their therapeutic efficacy and provided sustained release of the drug over a period of time. These results demonstrate that the developed system is an alternative to conventional drug delivery system, patient compliance, industrially oriented and economical.

Keywords: In situ, film, methylcellulose, gelation, hydrocortisone and ulcer

Introduction

Over the past 30 years greater attention has been focused on development of sustained release1, sustained action, prolonged action, controlled release, extended release and depot release dosage form are the terms used to identify drug delivery system that are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose of a drug and become the standard in modern pharmaceutical design2.An intensive research have been undertaken in achieving much better drug product effectiveness reliability & safety.

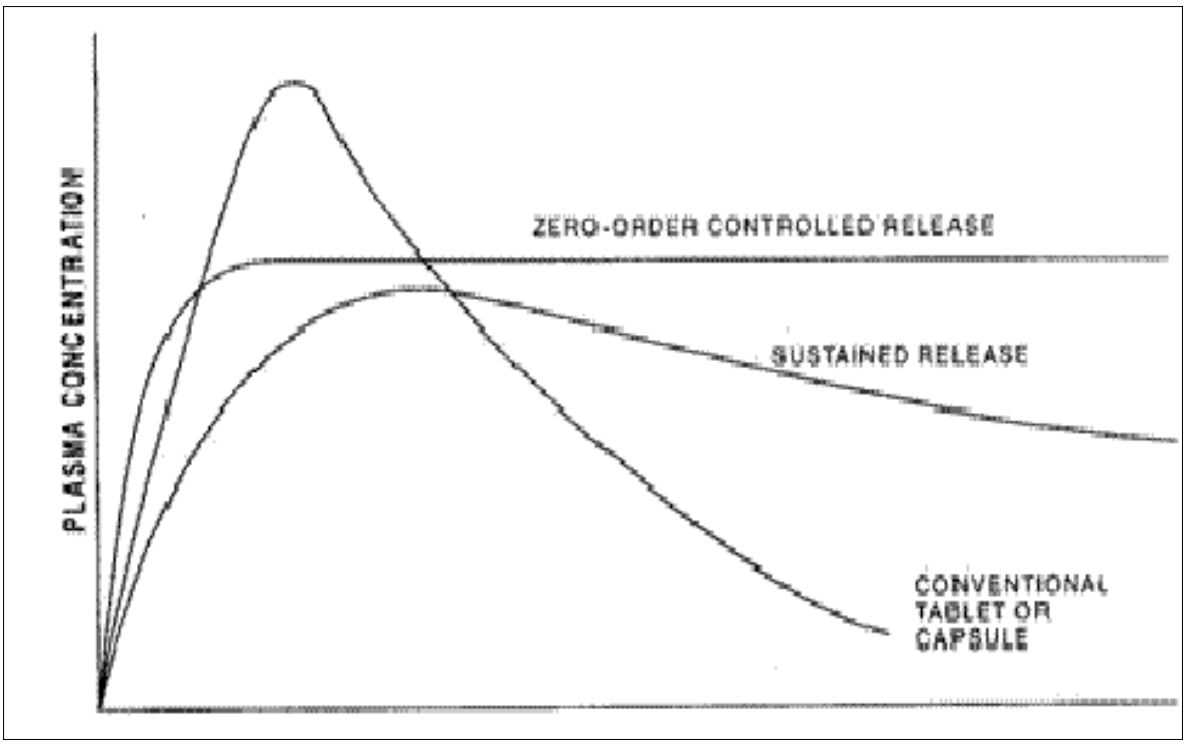

Fig 1: Plasma concentration behaviour.

Sustained release system include any drug delivery system that achieves slow release of the drug over an extended period of time. If the system is successful in maintaining control drug level in the blood or target tissue it is considered as controlled release system. If it is unsuccessful at this but nevertheless extends the duration of action over

that achieved by conventional delivery, it is considered a prolonged release system3. The oral route of administration for sustained release system has received greater attention because of more flexibility in dosage form design. The design of oral sustained release delivery system are subject to several

Inter: related variables of considerable importance such as type of delivery system the disease being treated, the patient, the length of therapy and the properties of drug

Materials and methodology

1. Method

Table 1: List of Materials

S. No	Ingredients	Company Name
1	Hydrocortisone	Yarrow chem. Products, Mumbai
2	Methyl cellulose	S.D Fine Chem. Ltd, Mumbai
3	Sodium citrate	S.D Fine Chem. Ltd, Mumbai
4	Propylene glycol	S.D Fine Chem. Ltd, Mumbai
5	Tri-ethanol amine	S.D Fine Chem. Ltd, Mumbai
6	Electronic Balance	Citizen, India.
7	Magnetic stirrer with hot plate	Almicro, Bangalore.
8	UV-Visible Spectrophotometer	Shimadzu UV"1800, Japan
9	FT-IR Spectrophotometer	Thermo Nicolet 380, India
10	Digital pH meter	Chemi line.
11	Brook field viscometer	RV DV2 T, India.
12	Stability chamber (106 Model)	LABTOP, SKY Lab Instruments & Engineering Pvt. Ltd
13	Dissolution chamber	LABINDIA, DS 8000, India
14	SEM	FEI Quanta 200 F.
15	DSC	DSC 4000.
16	Electronic Balance	Citizen, India.
17	Magnetic stirrer with hot plate	Almicro, Bangalore.

2. Preformulation studies of drug

- Determination of melting point
- Solubility
- Determination of λ_{max}
- Compatibility *study*

Selection of vehicle

Formulation design

Evaluation

- pH
- *In vitro* gelation studies & viscosity
- Drug content
- Spreadability
- Tensile strength
- Folding endurance
- Disintegration studies
- *In vitro* drug release study
- Ex – *Vivo* study
- Stability studies

Results and discussion

1. Drug solubility studies

Drug solubility studies have done by using various solvents. Solubility of Hydrocortisone was found to be in methanol. Results have showed that Hydrocortisone is highly soluble in methanol. It has high solubility in methanol than other solvents and poorly soluble in water compared to acetone.

2. Determination of λ_{max}

The λ_{max} of Hydrocortisone was found to be 242 nm in methanol.

3. Calibration curve of Hydrocortisone

The absorbance was measured in a UV spectrophotometer (Shimadzu UV"1800) at 242 nm in methanol. The absorbance so obtained was tabulated as in Table 7. Calibration curve was plotted as shown in the figure 2.

Table 2: Calibration data of Hydrocortisone

SL. no	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	0.5	0.132
3	1	0.256
4	1.5	0.412
5	2	0.591
6	2.5	0.772
7	3	0.883

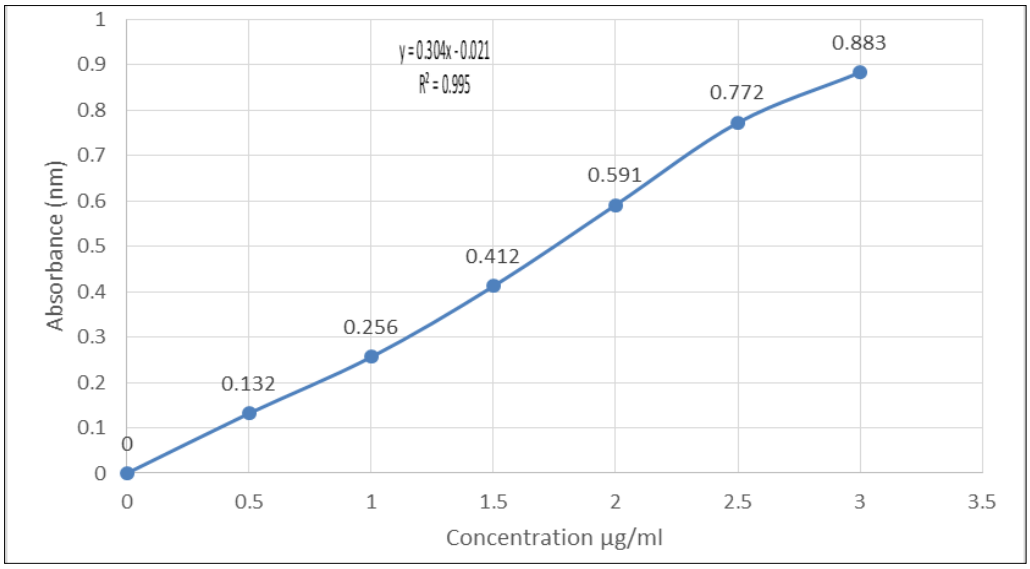

Fig 2: Calibration curve of Hydrocortisone

4. FT-IR spectrum

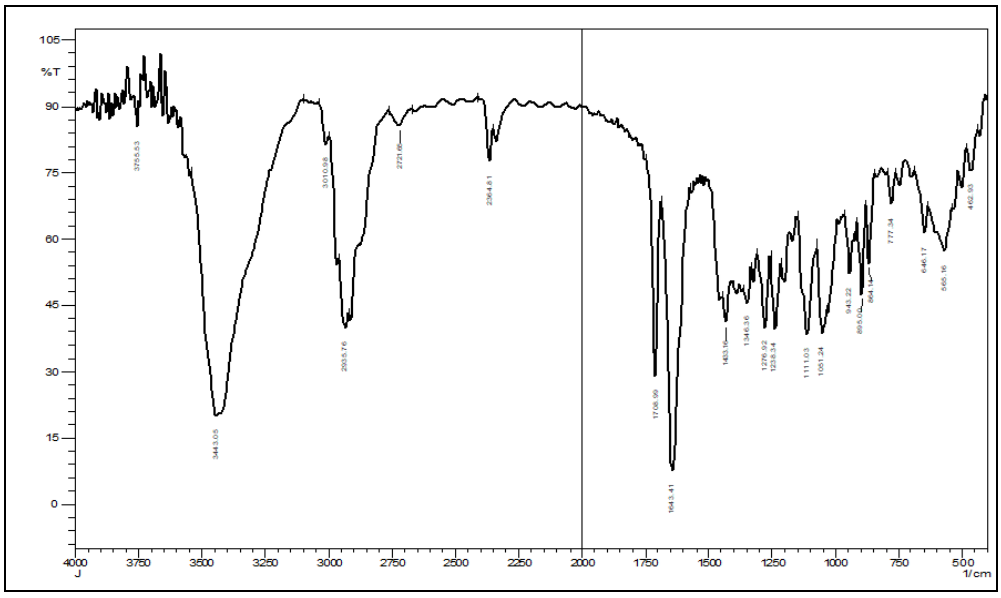

Fig 3: FT-IR spectrum for pure drug

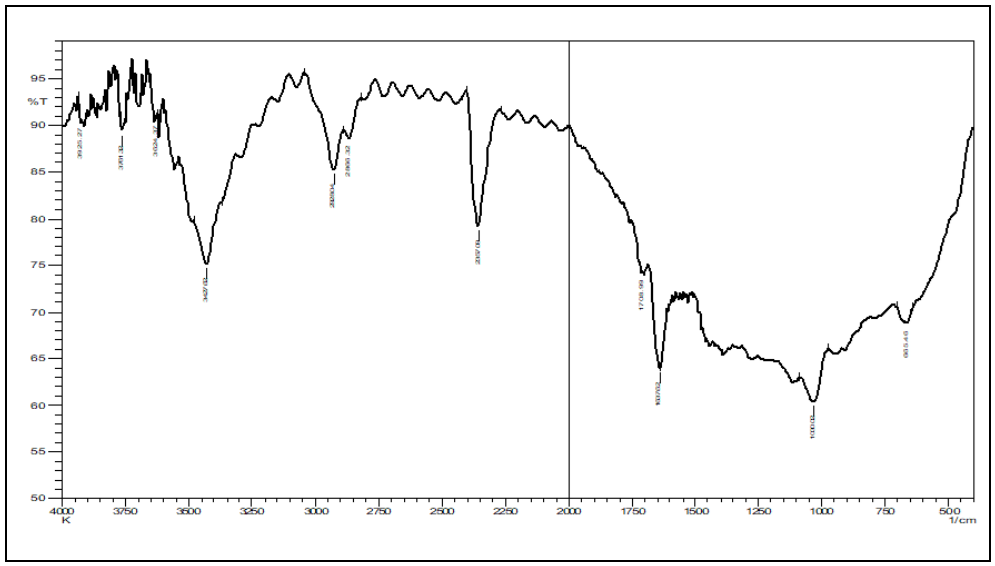

Fig 4: FT-IR spectrum for pure drug with polymer

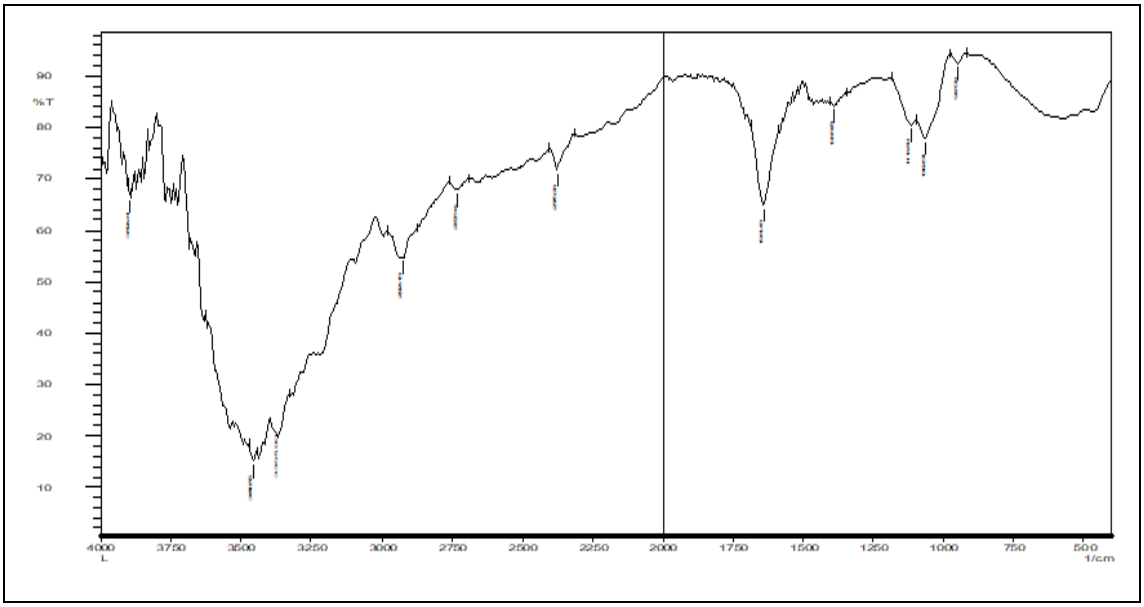

Fig 5: FT-IR spectrum for *in situ* gel formulation

5. Drug content

The drug content estimation was done and the absorbance were measured by UV spectrophotometer (Shimadzu UV"1800), drug content was calculated (Table 14). Drug content of all formulations was found between 76.4±0.051 to 97.6±0.093 w/v.

Table 3: Drug content of *in situ* gel

Formulation Code	Absorbance (nm)	Conc. of drug µg/ml	% of Drug
F1	0.206	0.700	80.3±0.012
F2	0.196	0.66	76.4±0.051
F3	0.208	0.707	81.1±0.076
F4	0.217	0.738	84.7±0.082
F5	0.250	0.850	97.6±0.093
F6	0.218	0.741	85.1±0.091
F7	0.247	0.840	96.4±0.097
F8	0.243	0.826	94.8±0.066

6. Scanning electron microscopy of oral film

One of the oral film formulations was subjected to SEM studies to assess changes in its surface morphology (Fig.). Initially prepared film revealed smooth and compact surfaces but, after dissolution studies, the film appeared porous and showed significant changes in texture and clearly visible pores. This might be due to the uptake of water resulting from the presence of methylcellulose in the formulations. Based on these results, it can be concluded that the methylcellulose in patches absorbs water and significantly affects their surface morphology and leads to the formation of pores in accordance with the *in vitro* dissolution data.

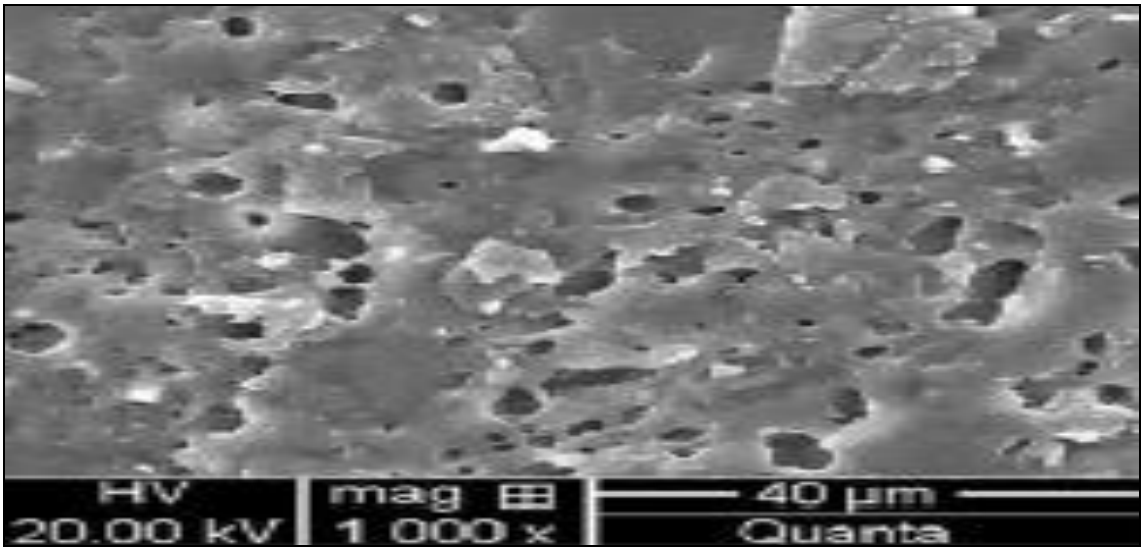

Fig 6: SEM image of oral film

7. Stability studies

Table 4: Stability studies of oral films stored at 40 ±1°C/ ambient humidity

No. of days	Drug content%							
	F1	F 2	F 3	F 4	F 5	F6	F7	F8
15	93.75	93.2	94.52	95.61	98.48	96.09	97.6	96.8
30	93.73	93.19	94.50	95.59	98.47	96.07	97.59	96.78
45	93.71	93.17	94.49	95.58	98.46	96.05	97.58	96.76
60	93.70	93.16	94.47	95.56	98.44	96.04	97.66	96.74
75	93.68	93.15	94.46	95.54	98.42	96.01	97.64	96.73
90	93.66	93.12	94.45	95.52	98.40	96	97.62	96.71

Conclusion

The present work is an attempt to develop a in situ gels and films of Hydrocortisone from temperature induced gelling system. The study has demonstrated various aspects and from the results obtained, it was concluded that

- In situ gel formulation of Hydrocortisone with mucoadhesive properties is useful to prolonging residence time in mouth.
- The developed formulation can release the drug at controlled rate for prolonged duration.
- Local drug delivery may be an advantageous in treatment, since it would probably eliminate side effects, which occur with systemic dosing.
- Effective and prolonged release of drug could be achieved without much systemic load with comparatively less frequency of administration.
- This type of drug delivery system can serve as a novel approach for treating mouth infections with better patient compliance.
- The optimized formulations F5 (Methylcellulose 1.25%), F6 (Methylcellulose 1.50%), F7 (Methylcellulose 1.75%) were liquid before instillation into mouth and underwent rapid gelation upon instillation into mouth.
- The formulations were found to be clear, having good in situ gelling capacity and a drug content 84-96%.
- Optimised formulations were sterile and showed sustained drug release over 8 hrs.

Acknowledgments

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