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Formulation, Evaluation, Development, Characterization, and *In Vitro* Evaluation of Sulfasalazine hydrogel for the treatment of Oral Lichen Planus

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ABSTRACT: Sulfasalazine topical hydrogel is a type of s medicine applied directly to the skin to reduce inflammation, irritation, and pain. Topical Sulfatase hydrogel is useful against the use of corticosteroids. Sulfasalazine, an anti-inflammatory drug, has limited solubility in both aqueous and organic solvents. Achieving its effective dispersion within the hydrogel matrix poses a significant challenge. To overcome this hydrogel was prepared by using modifying polymers, Carbopol 934 P. Physicochemical properties of the drug were evaluated by ultraviolet, Fourier transforms infrared spectroscopy (FTIR), and solubility study. Hydrogel appearance clarity, pH, viscosity, extrudability, rangeability, drug content, surface pH, in vitro drug release, Ex vivo permeability, stability study histopathology study, and release of kinetics model. The FTIR studies showed no evidence of interactions between drugs, polymers, and excipients. Formulation F4 achieves an in vitro drug release of 81.67% ± 0.28 at 2 h and fine evaluation results. We successfully developed hydrogel formulations of Sulfasalazine and describe an effective result for the treatment of OLP for resistance to corticosteroid therapy.

Keywords: Sulfasalazine, Hydrogel, Ulcer, Fibroblast, *In-Vitro* ulcer.

INTRODUCTION

First described in 1869 by British physician Wilson Erasmus, lichen planus (LP) is an autoimmune condition present on the skin, hair, eyes, mucous membranes, and nails. Oral lichen planus is a painful Oral lesion that may develop in the mucous membrane of the mouth and are most frequently sore. The present research is aimed to develop a gel of Sulfasalazine for the treatment of Oral Lichen Planus. Hydrogel was prepared by using different concentrations of powdered Sulfasalazine and Carbopol 934, and Propylene glycol as a gel base (Pakravan, 2006). The prepared formulations were evaluated for better consistency using gelation temperature, gelling capacity, pH, viscosity, syringe ability, spreadability, drug content, and In vitro and ex vivo studies. The formulations' drug content (76.40–94.7%) was reasonably homogeneous, and their pH value was 6.8. In. In vitro drug release was carried out for 8 h using phosphate buffer as a diffusion medium. 1% w/v of Sulfasalazine a gel base gives prolonged the drug release up to 8 h and showed sustained release behavior, with a very fine effect.

The oral mucosal surface is rich in blood supply and offers several advantages over both injectable and enteral methods of drug delivery. It is also an alternative method for systemic drug delivery. The oral mucosa absorbs substances at a rate that is around four times that of the skin. Developed gel displays enhance the bioavailability of medications. Studies on short-term stability were conducted, and no significant alterations were found. For the treatment of oral ulcers, developed herbal formulations were more reliable, secure, and efficient than synthetic formulations.

The National Oral Health Program was established by the Indian Dental Association (IDA) to promote "good oral health" for all people by the year 2020 while reducing the burden of dental problems. This has now been acknowledged as a crucial aspect of overall wellness (Boorghani *et al.*, 2010; Hijazi *et al.*, 2022). Food is a big modifiable factor that has a substantial impact on dental health. Dental health might suffer from an uneven dietary situation, and vice versa. Malnutrition may result from poor food intake, which can be influenced by poor dental health. Interdisciplinary teams made up of general doctors, dentists, nurses, and nutritionists have recognized the importance of oral health in connection to overall welfare and quality of life. These teams make certain that patients are well-fed and have a clean dental history. Oral lichen planus is a persistent (chronic) inflammatory condition that affects the mucous membranes of your mouth (LIE-kun PLAY-nus). Canker sores can appear as open sores, red, swollen tissue, or white, tired patches. These lesions may cause burning, pain, or other discomfort. Scaly lichen cannot spread from person to person. The disorder occurs when the immune system attacks the cells of the oral mucosa for unknown reasons. It is not known what

causes oral planus. However, in oral lichen, T lymphocytes, specific white blood cells associated with inflammation, are activated. This can be a sign of an immunological problem and there can be genetic influences. However, determining the exact cause requires further research. There are several possible causes of LP/OLP, but the most common are lichen-causing medications and dental products. If the lesions disappear when the pathogen is removed, this confirms the reaction of the lichen. If lesions persist, a diagnosis of LP/OLP is made (Pakravan, 2006; Rakesh *et al.*, 2018). Lichen planus appears in many different ways. The most typical symptoms are white spots on the oral mucosa (usually on the cheeks, tongue, and gums). They are usually not painful, but sometimes, in addition to the white spots, there can also be redness, ulcers, or, very rarely, blisters. If so, eating hot or spicy food may cause discomfort. The etiology of aphthous ulcers remains unclear. Other possible factors include trauma, drugs, lack of vitamin B12, folic acid, iron, stress, hormonal changes, and metabolic diseases (Bohra *et al.*, 2015). Sulfasalazine has been proposed as a therapeutic option with no significant side effects in the treatment of LP (Sung-Hee Jeong *et al.* 2016). Oral lichen stomatitis is a condition characterized by single or multiple painful ulcers of varying size and duration, usually affecting non-keratinized oral mucosa. When administered orally, sulfasalazine is metabolized to 5-ASA and sulfapyridine by azoreductase in the gut microbiota. Among various bacteria, *Lactobacillus acidophilus*, Bifidobacterium lactis, and *Streptococcus salivarius* have azoreductase activity. First, sulfasalazine is administered orally to treat oral planus. The treatment solution contained 30 mg of sulfasalazine in 5 ml of distilled water and administered three times a day for 3-5 minutes followed by coughing. Patients were prohibited from taking other medications and asked not to eat or drink for 30 minutes afterward (Lee *et al.*, 2012).

MATERIALS AND METHODS

Sulfasalazine was obtained from Yarrow Chem. Products Ltd, Mumbai; triethanolamine and sodium citrate were obtained from S.D. Fine Chemicals, Mumbai. All other chemicals and reagents used were of analytical grade.

1. Preformulation study

Melting point determination. The melting point of Sulfasalazine, Cp-930p, EDTA, TEA, and Mg stearate was determined by the capillary method. Using a small dry capillary tube that was sealed at one end, the substance whose melting point was to be determined was dried and added to form a compact column. The capillary was then tied to a thermometer and introduced in Thiele's tube. Heating was then started at the rate of an increase in temperature of 3 C per minute. Heating was continued until the substance was melted. At this stage, the thermometer reading was noted down (Jeličić *et al.*, 2021; Jadhav *et al.*, 2011).

Solubility. The solubility of Sulfasalazine was determined by adding an excess amount of Sulfasalazine in solvent (water and pH 6.7 phosphate buffer) at room temperature and occasional shaking for 24 h. Equilibrium solubility was determined by taking supernatant and analyzing it at a wavelength of 359 nm using a UV double beam spectrophotometer (Shimadzu 2450 PC, Tokyo, Japan) (Costa *et al.*, 2015; Shankar *et al.*, 2018; Mandal *et al.*, 2012).

Loss on drying: Loss on drying (LOD) of TM was performed by taking 1 g (W1) of Sulfasalazine into a weighed flat and thin porcelain dish11. It was dried in an oven (Bio Technics, Mumbai, India, BTI 10) at 105 C for 1 h. After cooling in desiccators, the sample of Sulfasalazine has weighed again (W2). Using the following formula, the % LOD was calculated (Eqn.1)

$$\%LOD \text{ ¼ } W1 \times W2 = W1 \times 100 \ldots\ldots\ldots\ldots \text{ Eqn.1}$$

Calibration curve of Sulfasalazine in Phosphate buffer pH 7.4

Preparation of standard stock solutions. Take 5 ml of methanol in a volumetric flask of 10 ml. Add 10 mg sulfasalazine to it. Dissolve it and add a quantity of sufficient water in it to prepare a stock solution containing 1 mg/ml of SF (Yasir Mehmood *et al.*, 2017).

NaOH solution (1 M): An amount of 8 g of NaOH was placed in a 200 ml volumetric flask and dissolved in distilled water, then the solution was completed to the mark.

Pure sulfasalazine solution (1×10^{-3} M): An amount of 0.08 g of sulfasalazine was dissolved in distilled water by placing it in a 200 ml volumetric flask then the distilled water and a few drops (3 drops) of NaOH (1 M) were added and the solution was completed to the mark.

Construction of calibration curve. The calibration curve of the sulfasalazine-NQS product at optimum conditions and maximum absorption (359 nm). The solutions were prepared by taking 3 ml of each concentration of drug and reagent (within the range 1 to 30×10^{-5} M) then placed in a 10 ml volumetric flask and the pH was adjusted to 12.5 by adding buffer solution. Solution preparation is done according to Table 5 and the solution was completed to the mark (10 ml). It was found that Beer's law complied within the concentrations range (1-25) $\times 10^{-5}$ M. The molar absorptivity was 1.438×10^{4} L mole^{-1}. cm^{-1}. Other statistical parameters such as average recovery, relative standard deviation (RSD), the limit of quantitation (LOQ) and limit of detection (LOD), Sandel sensitivity, and molar absorptivity, as shown in graph Fig. 1.

2. Formulation and development of gel

Preparation of gelling system. A sufficient amount of Carbopol 934 was soaked in distilled water overnight and then mixed with distilled water with continuous stirring using a mechanical stirrer. Another solution containing varying concentrations of EEA, EEO, and EEZ and the required quantity of methyl paraben and propyl paraben were added with continuous stirring. Propylene glycol was also added to the solution. This prepared solution was further mixed with Carbopol 934 solution thoroughly with continuous stirring, the volume was made up to 30 ml with water, and the pH was adjusted by the addition of triethanolamine to obtain gel of the required consistency. Seven formulations (F1 to F7) of the herbal gel were prepared (Kaur *et al.*, 2004). As indicated in Table 1.

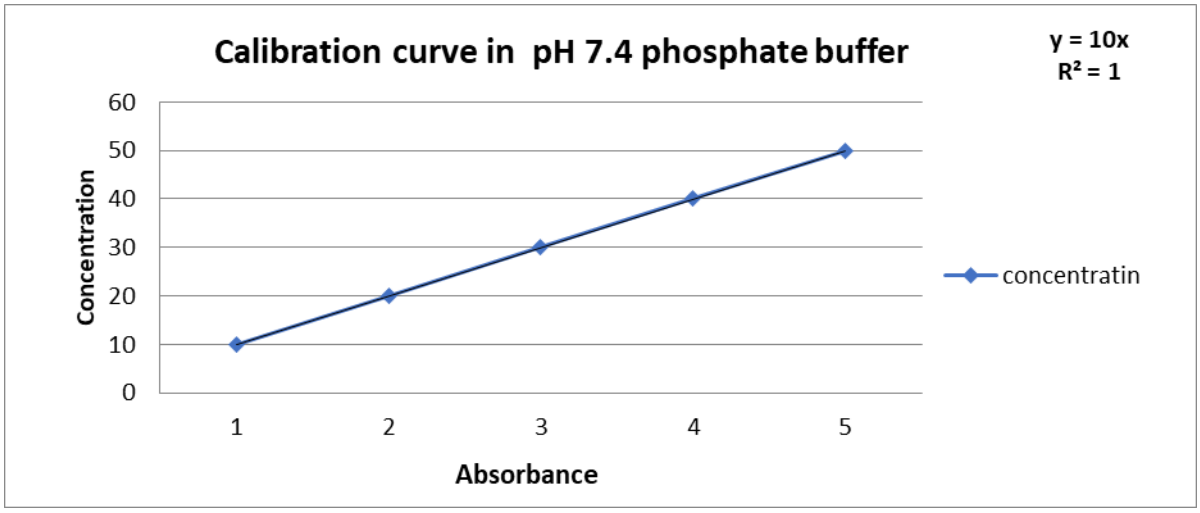


Fig. 1. Calibration curve in pH 7.4 phosphate buffer.

Table 1: Compositions of the formulations sulfasalazine hydrogel with different Carbopol 934 grade polymer concentrations) (% w/w).

Sr. No.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
1.	Sulfasalazine	1000	1000	1000	1000	1000	1000	1000	1000
2.	Carbopol 934	**0.1%**	**0.2%**	**0.3%**	**0.4%**	**0.5%**	**0.6%**	**0.7%**	**0.8%**
3.	Propylene glycol	5ml	5ml	5ml	5ml	5ml	5ml	5ml	5ml
4.	EDTA	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
5.	TELA	1.5ml	1.5ml	1.5ml	1.5ml	1.5ml	1.5ml	1.5ml	1.5ml
6.	Glycerine	2ml	2ml	2ml	2ml	2ml	2ml	2ml	2ml
7.	Water (Q.S)	100	100	100	100	100	100	100	100

Appearance, clarity and pH. The prepared gels were tested for color, clarity, texture, transparency, and the presence of any gritty particles. Appearance and clarity were visually recorded in the light before and after gelling against the white and black backgrounds as in Table 3.

The pH of herbal gel formulations was determined by using a digital pH meter. 1 gm of gel was taken and dispersed in 10 ml of distilled water and kept aside for two hours. The measurement of the pH of formulation was carried out three times and the average values are reported. the pH of the gel formulation was reported. The pH one of the most important parameters for gel formulation was directly measured using a digital pH meter (Deluxe pH meter, India) (Aiyalu *et al.*, 2016).

Viscosity. Brookfield optical viscometer (RVDV2 T model) was used to assess the viscosity and the-related properties of in-situ gel hydrocortisone using T-96 spindle. Taking 50 g of the gel in a beaker, the spindle was dipped inside. The gel viscosity was measured at varying angular velocities at 25 C. A normal course was for the angular velocity to change from 5 to 25 rpm (Baloglu *et al.*, 2011; Patel *et al.*, 2014), as per Table 4.

Syringe ability. All prepared formulations were transferred to the constant volume (2 ml) of a 5 ml syringe placed with a 20-gauge needle. The solutions, which were quickly passed from the syringe, were called passing and difficult to pass, as failed (Baloglu *et al.*, 2011; Patel *et al.*, 2014).

Spreadability. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel that is placed in between the slides under the direction of a certain load. If the time taken for the separation of two slides is less then better the spreadability. Spreadability is calculated by using the formula: $S = M \times L / T$ Where M = weight tied to the upper slide L = length of glass slides T = time taken to separate the slides (Fong Yen *et al.*, 2015; Basha *et al.*, 2011), results are given in Table 4.

Extrudability. In this test, a sample is extruded from the tube by the usual procedure. A closed collapsible tube containing gel was passed firmly at the crimped end. When the cap was removed, the gel extrudes until pressure dissipated. The weight in grams required to extrude a 0.5 cm ribbon of gel in 10 seconds was determined. The results for each formulation were recorded as extrusion pressure in grams to the percentage of gel extruded from the tube (Basha *et al.*, 2011; Kumar & Verma *et al.*, 2010; Tiwari *et al.*, 2021).

Drug content analysis. The weighed amount of gel equivalent to 2 mg of the drug was accurately taken and dissolved in phosphate buffer (pH 6.8). The product content was measured against phosphate buffer at 359 nm (pH 6.8) using UV Visible Spectrophotometer-1800 (Shimadzu, Japan) and determined from the calibration curve (Harish *et al.*, 2009; Melo *et al.*, 2009).

***In vitro* drug release studies**

The study of Sulfasalazine gel in vitro drug release from the in-situ gel formulations was conducted using a cellophane membrane for a period of 8 h. Phosphate buffer was the dissolution medium of pH 6.8. Tied to one end of a glass cylinder was the cellophane membrane, previously soaked overnight in the

dissolution medium. Then 1 ml of the formulated formulation was wrapped in a cellophane membrane and placed in a phosphate buffer. The dissolution medium was stirred with a magnetic stirrer at 50 rpm. The sample was collected at regular intervals and replaced by a receptor medium volume similar to that. At the time interval predetermined, one ml of the sample was taken and spectrophotometrically analyzed at 359 nm (Walewijk *et al.,* 2008; Zaki *et al.,* 2022). Detail analysis parameters are indicated in Table 7.

Drug release kinetics. To understand the drug release kinetics of in situ gel formulation of hydrocortisone, the data on drug release were treated with zero order, first-order kinetics, and the equation of Higuchi. The release mechanism was understood by fitting the data into the Korsmeyer-peppas equation Mt/Ma ¼, where 'Mt/Ma' is the fraction of the drug released at the time t,' 'K' is the kinetic constant, and 'n' is the release exponent that defined the process for releasing the drug. If the value of 'n' is less than 0.45 then it is considered a Fickian release, values greater than 0.45 and less than 0.89 are considered anomalous (non-Fickian) transport, and finally, the value of 'n' greater than 0.89 follows super case- II release mechanism. As per Table 9 (Walewijk *et al.,* 2008; Zaki *et al.,* 2022) all the details have been gin in Fig. 4 for reference.

Stability study. Stability analysis of optimal formulation was performed at 25 C/60% and 40 C/75% RH according to the State Guidelines of the International Conference of Harmonization (ICH). Refer to Table 11 for the same. Stable formulations were evaluated for pH, gelling ability, product quality, and rheological properties in vitro dissolution for three months (Ansari *et al.,* 2019 ; Meutia Sari *et al.,* 2021).

FTIR Study. The potential for drug-polymer interactions was assessed using FTIR (Jasco M 4100, Mumbai, India). KBr pellet method was used to spectroscopically analyze Sulfasalazine, polymer, and formulation these pellets were scanned from 4000 to 400 cm^{1} wavenumbers, and characteristic peaks were observed (Choi *et al.,* 1994; McGirt *et al.,* 2006), formulation pellets of carbazole with sulfasalazine is indicated in Table 6.

3. Ex vivo studies

Ex vivo release analysis was performed with fresh chicken skin which was soaked for 5–6 h in the sodium bromide solution and washed with water to extract the adhering fat tissue. The skin was then placed in the phosphate buffered diffusion cell (pH 6.8). as in Fig. 8. The medium was thermostatically controlled at a temperature of 37^{C} and 5 ml of the sample was collected at fixed intervals and spectrophotometrically measured at 359 nm against their respective blank formulation (Favia *et al.,* 2021; Cui *et al.,* 2023; Shaikh *et al.,* 2018).

4. Histopathologic evaluations

To determine the degree of epithelial regeneration of the ulcer tissue, the maximum diameter (ND) of the residual ulcer and the MD of the mucosal defect was measured. The percentage of MD after ND reduction was taken as the relative degree of epithelial regeneration of ulcers. In the control ulcers, the ND area was larger than in the gel group, which also showed a novel epithelium that covered the ulcer.

Observation has been provided in Fig. 7 and 8, The gel group showed higher epithelial regeneration than the control group (0.52 vs. 0.36, p0.031).

RESULT AND DISCUSSION

1. Preformulation Studies

Physical state. Sulfasalazine was physically examined for colour and odor etc. It was found to be white to light yellow, odorless, tasteless powder.

Melting Point Determination**:** The melting point of Sulfasalazine was found to be 220ºC±3°C.

Solubility Study. Solubility has been studied in different solvent media. Solubility studies showed the highest solubility in organic alkali hydroxide solutions and almost negligible in aqueous solutions. There was comparably more solubility in the basic media as well as in the phosphate buffer than in the acidic solution. Details of the solubility study have been shown in Table 2.

Table 2: Solubility study Of Sulfasalazine drug in different solvent media.

Concentration mg/ml	Solvent
Water	Practically insoluble
ethanol	Very slightly soluble in ethanol
Diethyl ether	Practically insoluble
chloroform	Practically insoluble
0.1N NaOH	Completely soluble

2. Formulation

Preparation of gelling system

Table 3: The appearance of different batches of Sulfasalazine hydrogel.

Formulation	Homogeneity	Color
F1	+++	Transparent
F2	+++	Transparent
F3	+++	Transparent
F4	+++	Transparent
F5	+++	Transparent
F6	+++	Transparent
F7	++	Transparent
F8	+++	Transparent
F9	+++	Transparent

(Excellent-+++, Good-++, Present-+)

FT-IR study. Formulations displayed typical peaks of drugs and polymers while no new bands or point changes existed suggesting no interaction between drugs and polymers. FT-IR studies showed the Sulfasalazine peaks at 3443 cm (OH stretching), 2936 cm (CH stretching), 1708 cm1 (COOH), 1643 cm1 (carbonyl group), 1433 cm1 (OH bending), and 1275 cm1 (C–O stretching). Characteristic peaks at 3427 cm1 (OH Stretching), 2928 cm1 (CH Stretching), 1708 cm1 (COOH), 1637 cm1 (Carbonyl), and 1033 cm1 (C–O–C Stretching) in both drug and polymer.

Table 4: Different evaluation parameters of Sulfasalazine hydrogel-pH, Spreadability, Extrudability, and Syringe ability.

Sr No.	Evaluation	F1	F2	F3	F4	F5	F6	F7	F8
1.	**pH**	6.6	6.4	6.7	6.9	6.8	6.9	6.8	6.7
2.	**Spredability (gm.cm/sec)**	11.93	12.70	9.18	11.36	12.30	10.63	13.94	11.76
3.	**Extrudability (%)**	82	93	86	92	90	96	89	93
4.	**Viscosity (Cps)**	18471	18211	19200	19420	20352	22144	22917	23163

Table 5: Calibration curve of Sulfasalazine in phosphate buffer.

Sr. No	Concentration (ug/ml)	Absorbance
1.	10	0.5032
2.	20	0.9648
3.	30	1.5661
4.	40	1.9778
5.	50	2.3774
	Equation of the line R2	Y=10x-0.0 1

Peaks at 3456 cm1 (OH Stretching) and 3365 cm1 (NH stretching), 2924 cm (CH Stretching), 1388 cm1 (OH Bending), 1641 cm1 carbonyl functional group, and 1114 cm1 (C–O–C stretching). This spectrum showed some drug functional groups were masked due to the encapsulation of polymer. Formulations displayed typical peaks of drug and polymers while no new bands or point changes existed suggesting no association between drugs and polymers. as shown in Fig. 2 and 3. There was no interaction formed after the physical mixture of drug and polymer. Thus it showed the physical compatibility of the drug with the polymers.

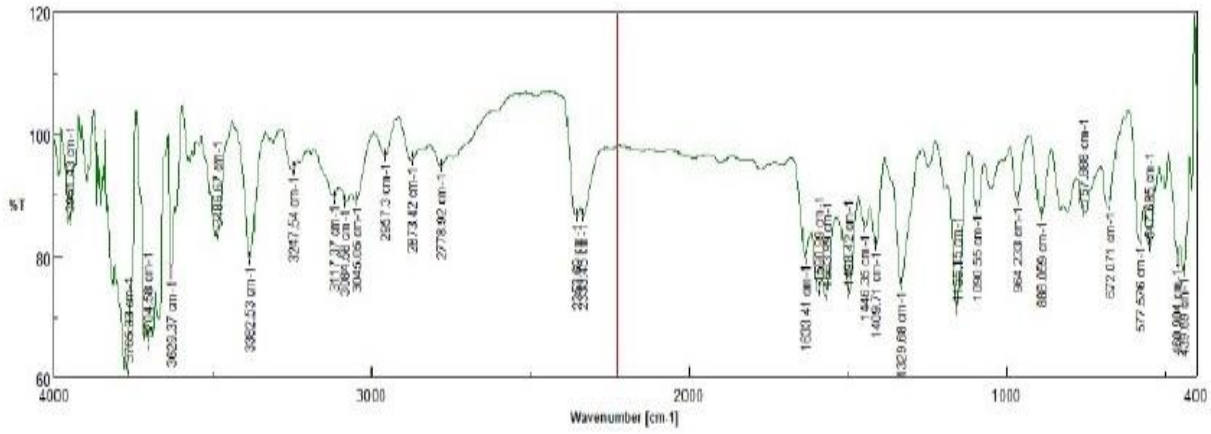


Fig. 2. Spectra of pure sulfasalazine drug.

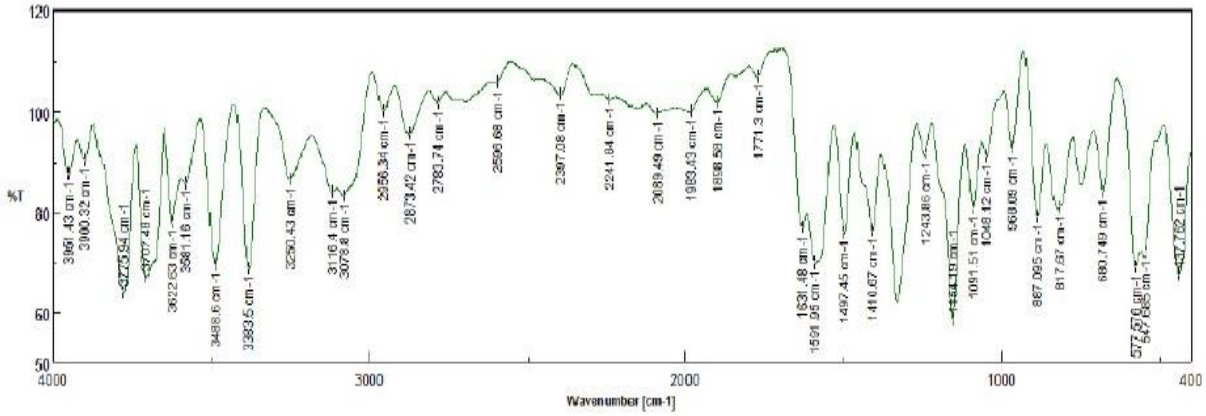


Fig. 3. FTIR Spectra of pure drug Sulfasalazine- Carbopol 934.

Table 6: FTIR parameters.

Standard Range	Observed Peak	Bond	Functional group
3300-2500	3250.43	O-H stretch	Alcohol
3350-3520	3383.5	N-H stretch	Amine
910-895	887.09	S=O	Sulfa
600-1400	680.749	C-N	Cyanide

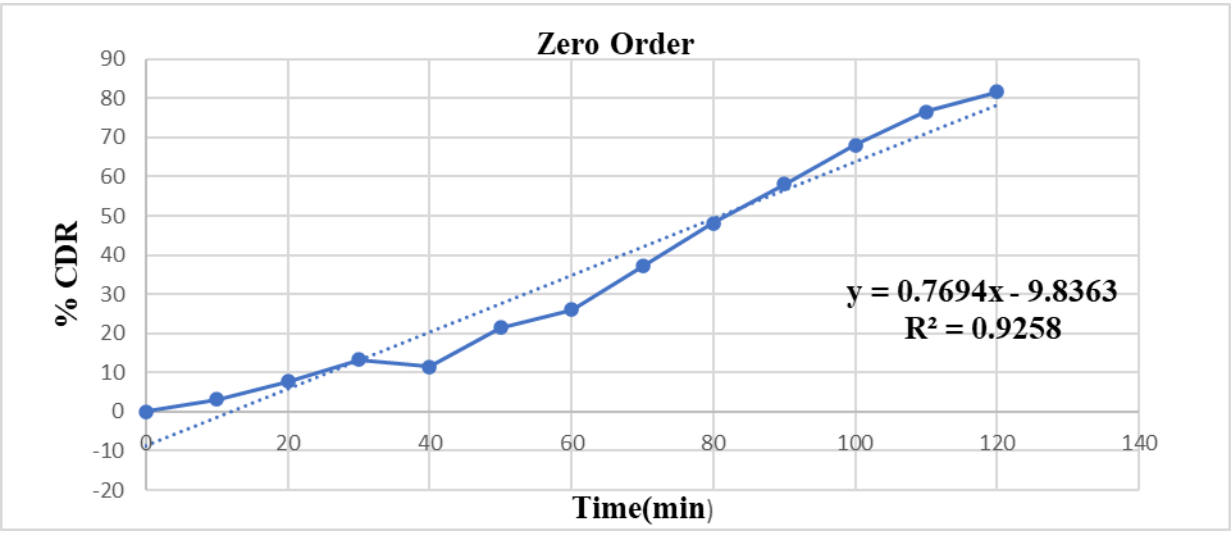
It showed that functional group peak frequencies of Sulfasalazine were in resemblance to the reported range of standard Sulfasalazine which authenticated that the obtained sample of Sulfasalazine was pure.

Table 7: In-Vitro drug permeation data for different formulation of Sulfasalazine hydrogel F1, F2, F3, F4, F5, F6.

Sr. No.	Time (Min)	(F1)	(F2)	(F3)	(F4)	(F5)	(F6)
1.	10	2.01	3.65	2.92	3.19	2.69	3.11
2.	20	3.21	8.46	6.77	7.65	7.53	6.52
3.	30	6.54	15.16	11.95	13.2	13.56	14.21
4.	40	17.41	19.24	19.36	21.49	19.36	17.93
5.	50	19.86	23.05	24.56	26.07	23.56	21.53
6.	60	23.69	37.18	35.71	37.11	28.93	27.63
7.	70	39.25	50.41	43.51	48.16	34.03	34.69
8.	80	49.26	54..99	49.52	58.97	41.22	41.22
9.	90	61.35	64.77	56.95	67.01	48.06	45.12
10.	100	74.48	63.7	63.73	74.12	54.89	48.75
11.	110	76.23	66.53	69.55	76.36	59.72	53.66
12	120	79.5	70.06	73.85	81.6	66.92	58.13

Table 8: Pure Sulfasalazine Drug content studies in buffer solution).

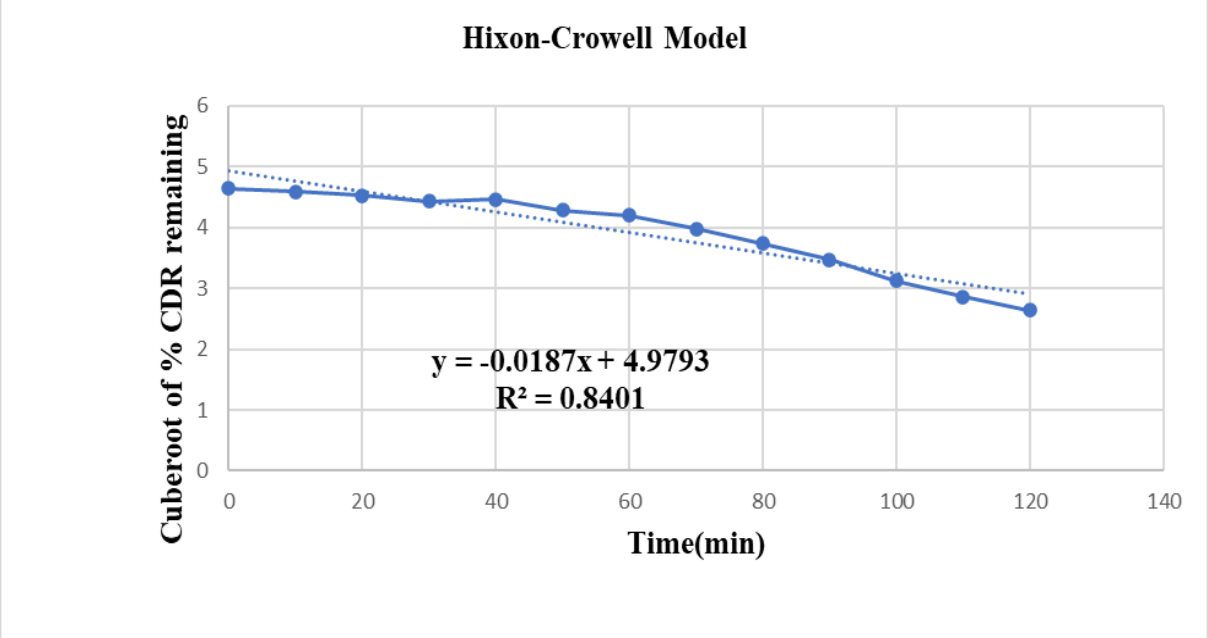
Sr. No	Formulation	Net Drug content
1.	F1	99.6%
2.	F2	88%
3.	F3	92.6%
4.	F4	101.%
5.	F5	103%
6.	F6	98%
7.	F7	96%
8.	**F8**	**99.2%**



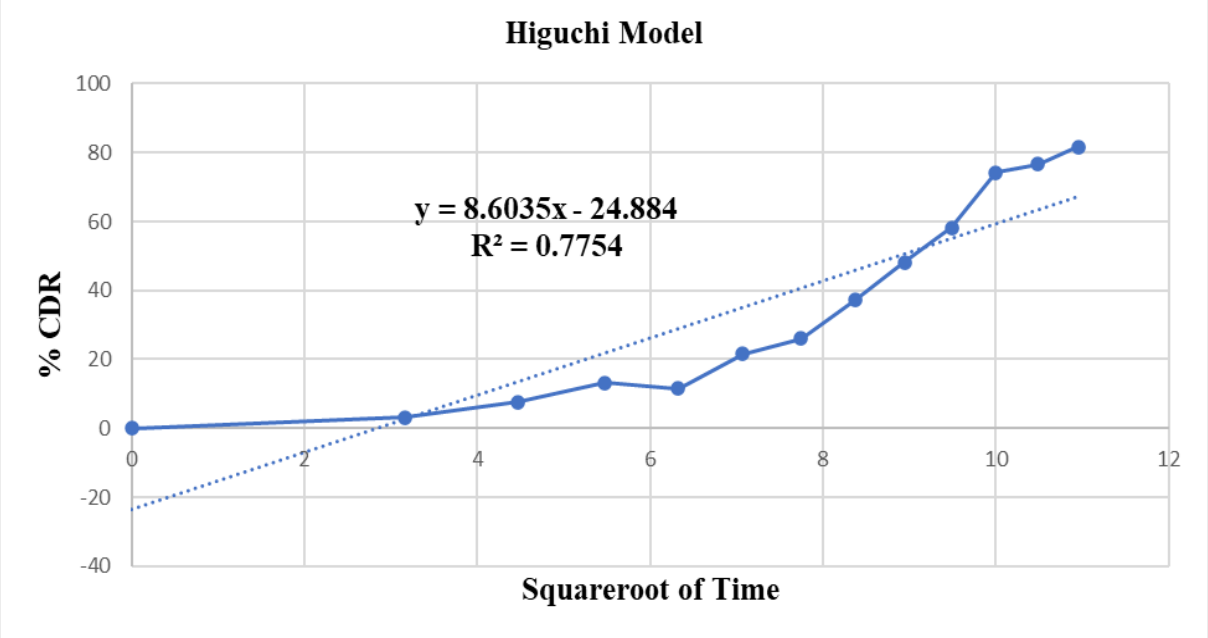
(a)


First Order
Log of % CDR remaining
2.5
2
1.5
1
0.5
0
0
20
40
60
80
100
120
140
Time(min)
y = -0.0069x + 2.1398
R² = 0.7797

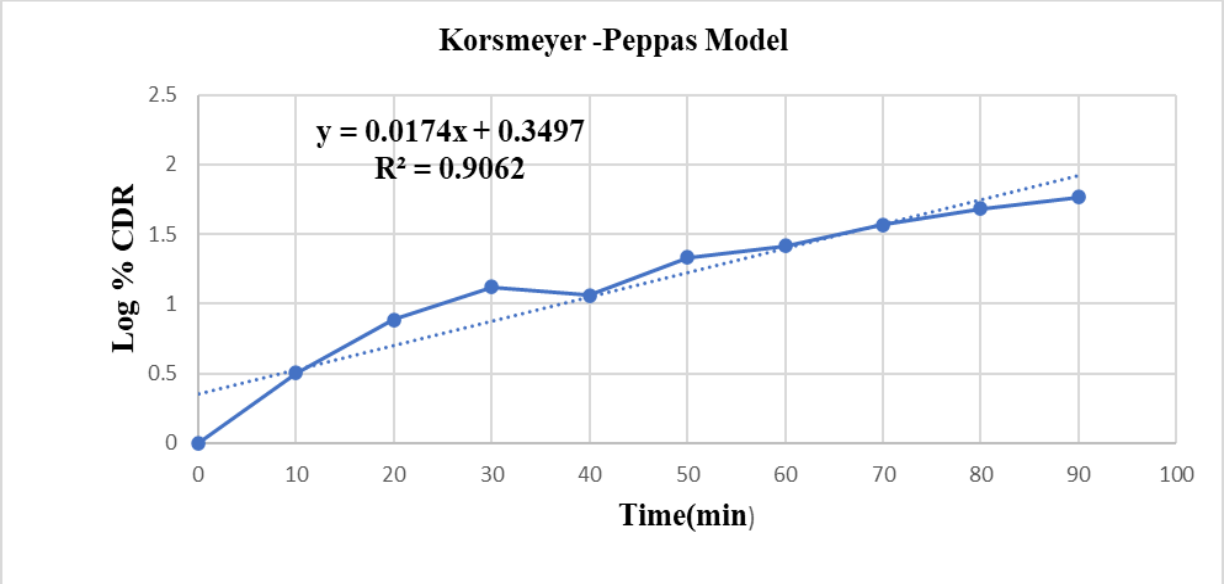
(b)


Hixon-Crowell Model
Cuberoot of % CDR remaining
6
5
4
3
2
1
0
0
20
40
60
80
100
120
140
Time(min)
y = -0.0187x + 4.9793
R² = 0.8401

(c)


Higuchi Model
% CDR
100
80
60
40
20
0
-20
-40
0
2
4
6
8
10
12
Squareroot of Time
y = 8.6035x - 24.884
R² = 0.7754

(d)



(e)

Fig. 4. Drug Release Kinetics for Sulfasalazine.

Table 8: Kinetics of drug release of formulated dosage form from F1 to F6 formulations.

Formulation	Zero Order		Fist Order		Higuchi		Hixon-Crowell		Korsemeyer-Peppas	
	R^2	$K_0(h^{-1})$	R^2	K_1(h-1)	R^2	$HC^{(h-1/2)}$	R2	$HC(^{h-1/3})$	R^2	n
F1	0.8589	5.5308	0.8907	-344.14	0.8201	4.905	0.8472	-0.0051	0.9465	0.0.241
F2	0.9342	5.5480	0.9539	-339.2	0.9037	4.946	0.9560	-0.0011	0.6788	0.239
F3	0.9439	5.4054	0.9523	-330.2	0.9065	4.8132	0.9179	-0.0011	0.9424	**0.249**
F4	0.9258	6.0859	0.7797	-221.03	0.7754	5.418	0.8444	-0.0015	0.9062	0.224
F5	0.9555	4.6924	0.9408	-330.24	0.9191	4.181	0.9466	-0.0009	0.9001	0.223
F6	**0.9665**	4.3106	**0.9539**	-305.27	**0.9326**	3.845	**0.9801**	-0.007	0.7676	0.232

Table 9: Different kinetics model for Sulfasalazine hydrogel.

Name Of Model	R2 Value
Zero Order	**0.9258**
First Order	0.7797
Higuchi Model	0.7754
Hixon-Crowell Model	0.8401
Korsmeyer-Peppas model	0.906

*The highest R2 value (0.9258) was shown by the zero-order Model, hence drug release confirms zero order model.

Table 10: General consideration of Sulfasalazine hydrogel of stability data color, odor, pH, viscosity, assay.

Formulation(F4)	Color	Odor	pH	Viscosity (cps)	Assay(%)
Room Tem	Transparent	Characteristic	6.7	17392	107.7
4	Transparent	Characteristic	7.1	18472	101.4
40	Slightly Yellow	characteristic	6.6	16318	**62.6**

Histopathology study.

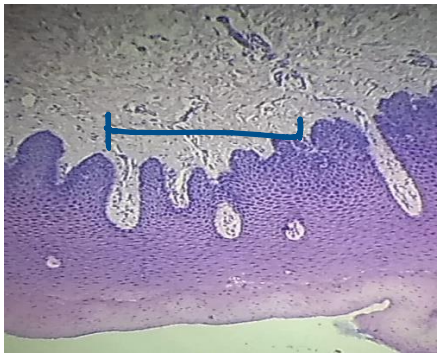


Fig. 5.

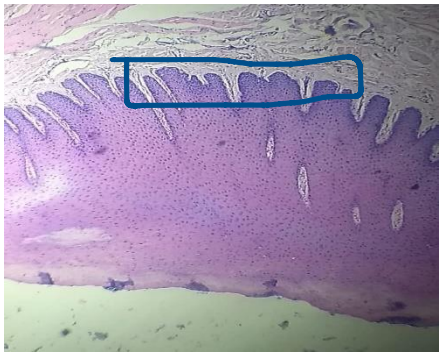


Fig. 6.

Histopathological examination showing epithelium regeneration. (A) The OLP of the control group had a large non-epithelial covering diameter. (B) The non-epithelial covering area of the gel-coated group was relatively small, in which new epithelium can be seen in the blue box.

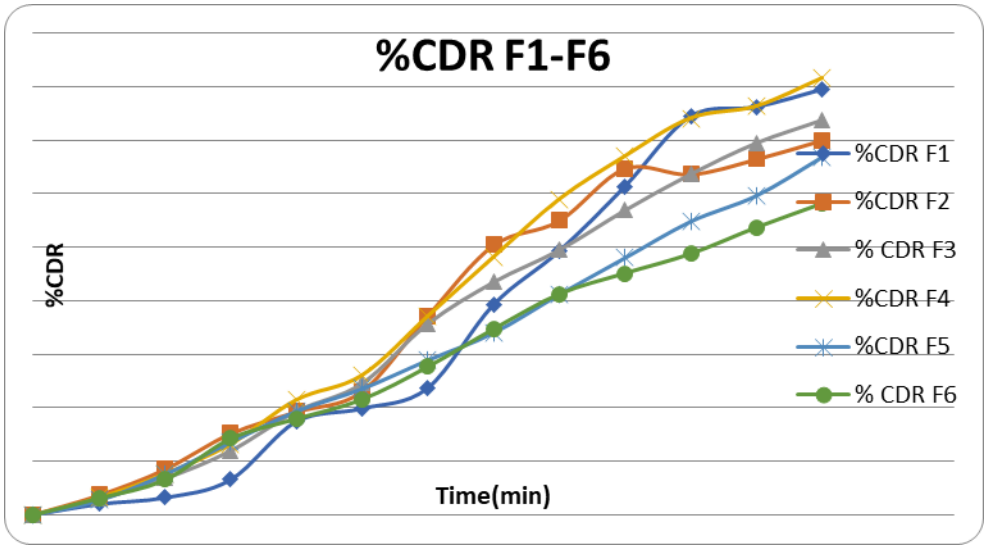


Fig. 7. *In Vitro* Drug Permeation Data For (F1, F2, F3, F4, F5, F6).

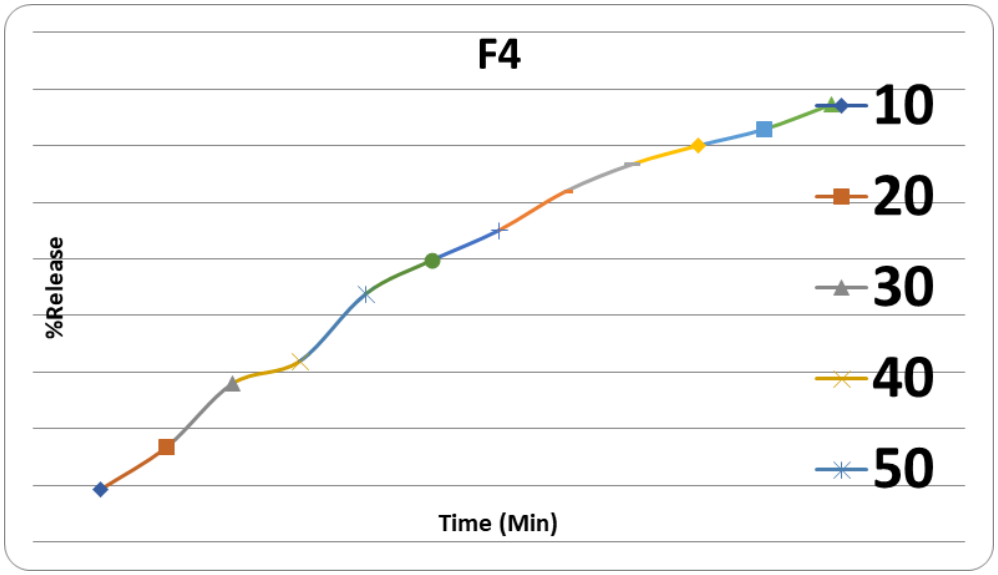


Fig. 8. Ex Vivo Study.

Table 11: Stability study parameters of Sulfasalazine hydrogel at different temperature.

Formulation (F4)	Color	Odor	pH	Viscosity (cps)	Assay(%)
Room Tem	Transparent	Characteristic	6.7	17392	107.7
4	Transparent	Characteristic	7.1	18472	101.4
40	Slightly Yellow	characteristic	6.6	16318	**62.6**

Stability Study. The research paper titled "Formulation, evaluation, development, characterization and *In Vitro* Evaluation of Sulfasalazine Hydrogel for the Treatment of Oral Lichen Planus" discusses the development and characterization of a hydrogel containing sulfasalazine, which is a potential therapeutic agent for the treatment of oral lichen planus. The authors aimed to formulate a stable, effective, and patient-friendly hydrogel that can be used for the topical treatment of oral lichen planus. The study was conducted using a variety of experimental methods. The hydrogel was formulated by dispersing sulfasalazine in the gel base, and the resulting formulation was evaluated for its physical properties, rheological behavior, drug release kinetics, and stability. The in vitro efficacy of the hydrogel was also evaluated using human gingival fibroblasts.

The results of the study showed that the sulfasalazine hydrogel had good physical properties, including a pH value of 6.8, and a viscosity of 23,168 cps. The hydrogel also exhibited shear-thinning behavior, which means it can be easily applied to the affected area and will not drip. The drug release kinetics showed that the hydrogel had a sustained release profile with 81.67% of the drug released for 2 hours. The in vitro studies showed that the hydrogel had a cytotoxic effect on human gingival fibroblasts, which suggests that it may be effective in treating oral lichen planus.

The study provides important insights into the development of a potential therapeutic agent for the treatment of oral lichen planus. The hydrogel containing sulfasalazine was found to be stable, effective, and patient-friendly, which makes it a promising candidate for topical treatment. The sustained release profile of the hydrogel could provide a prolonged therapeutic effect, which could improve patient compliance and reduce the frequency of application.

In conclusion, the study provides a foundation for further research into the development and clinical evaluation of sulfasalazine hydrogel for the treatment of oral lichen planus. The hydrogel showed promising physical properties and drug release kinetics, and the in vitro studies suggest that it could be an effective therapeutic agent for this condition. Further research is needed to evaluate the safety and efficacy of the hydrogel in animal and human trials.

CONCLUSION

Thus stable, effective gels containing Sulfasalazine along with ingredients for the management of mouth ulcers can be developed. In conclusion, this study strongly suggests the simplicity and practicality of the new gel. The use of this novel gel might provide shielding from the olp conditions, as reflected in promoting the speed of healing, enhancing epithelialization, and minimizing the use of corticosteroids.

FUTURE SCOPE

The future scope for the formulation, evaluation, development, characterization, and in vitro evaluation of Sulfasalazine hydrogel for the treatment of Oral Lichen Planus lies in conducting comprehensive clinical trials, optimizing the formulation for improved therapeutic properties and targeted drug delivery, investigating pharmacokinetics and biocompatibility, elucidating the mechanistic action, exploring personalized and combination therapies, ensuring long-term stability, and considering patient compliance and convenience, all of which will contribute to advancing the treatment of Oral Lichen Planus using Sulfasalazine hydrogel.

Conflict of interest. The author declares no conflict of interest in the research work.

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