Available online on 15.05.2026 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Research Article

Formulation and Evaluation of Rutin Trihydrate Topical Hydrogel

Amreen Mansuri, Dishant Gupta, Rajat Pawar *, P. K. Dubey, Sunita Patidar

Swami Vivekanand College of Pharmacy, Indore, India

Article Info:

Article History:

Received 23 Feb 2026
Reviewed 18 April 2026
Accepted 04 May 2026
Published 15 May 2026

Cite this article as:

Mansuri A, Gupta D, Pawar R, Dubey PK, Patidar S, Formulation and Evaluation of Rutin Trihydrate Topical Hydrogel, Journal of Drug Delivery and Therapeutics. 2026; 16(5):115-127 *DOI: https://dx.doi.org/10.22270/jddt.v16i5.7781*

For Correspondence:

Rajat Pawar, Swami Vivekanand College of Pharmacy, Indore, India

Abstract

Rutin, a naturally occurring flavonoid, has powerful anti-inflammatory, antioxidant, and vascular-protective effects, however it is poorly soluble in water and has low oral bioavailability. The current work sought to develop, optimise, and assess a topical hydrogel system containing rutin trihydrate to improve skin delivery and local therapeutic efficacy. Hydrogels were made with Carbopol 934 as a gelling agent and Transcutol-P as a cosolvent and permeation enhancer. UV calibration, solubility determination, and drug-excipient compatibility tests were all performed prior to formulation.Hydrogel batches were tested for physical appearance, spreadability, pH, viscosity, drug content, and in vitro release profile using Franz diffusion cells. The optimised hydrogel demonstrated desirable rheological qualities, good spreadability, pH within the skin-compatible range, high drug content, and improved release characteristics. In this study byusing Transcutol P and Carbopol 934, a topical hydrogel of rutin trihydrate will be created.Its viscosity, rheology, stability, and suitability for topical administration will all be assessed. By examining drug penetration through skin at various enhancer doses, it further explores Transcutol P's function as a skin-permeation enhancer.

Keywords: Rutin trihydrate, hydrogel, Carbopol 934, Transcutol P, topical drug delivery, skin.

1. INTRODUCTION:

Research has long focused on topical drug delivery because of its many proven benefits, including localized drug action, avoiding first-pass metabolism, and increased patient compliance due to its non-invasive nature and less systemic side effects. Notwithstanding these advantages, the stratum corneum, sometimes referred to as the horny layer, serves as a significant obstacle to the absorption of drugs via the skin. The effective distribution of active medicinal components from conventional formulations is frequently hampered due to the skin's barrier qualities. Consequently, in order to improve drug penetration and therapeutic effectiveness, there is an increasing need for appropriate carrier systems.[1]

The complicated etiology of skin diseases, the many adverse effects of traditional treatments, and the challenges in identifying the disease's main causes make treating them a tough and time-consuming process. Often, superficial wounds are simple to heal. However, professionals find it difficult to treat serious burn wounds. Site-specific distribution of medications at the appropriate moment for an extended period of time is the foundation for the best possible therapeutic outcomes. Frequent dosing and systemic toxicity are the two main issues with using traditional therapies. The preferred medium for drug delivery is hydrogel due to its excellent biocompatibility and capacity to both retain and release therapeutic chemicals.[2] To create biomaterials that improve or restore tissue function, the multidisciplinary area of tissue engineering (TE) combines the living sciences and engineering. Biocompatible and biodegradable scaffolds are essential components of TE; they are extremely porous three-dimensional structures that promote tissue regeneration, cell proliferation, and differentiation. Cells, growth hormones, or medications are frequently included into these scaffolds to enhance therapeutic results. One of the main goals is to imitate the extracellular matrix (ECM), which gives regeneration biochemical and mechanical cues. Even with TE's promise, there are still issues with processing and material selection. Because of their ECM-like qualities—such as their high water content, flexibility, and biocompatibility—hydrogels have drawn interest and are hence perfect for use in biomedical applications.Hydrogels are presented as a promising solution for a number of well-known potential applications, including wound healing and controlled medication release[3]

Hydrogels are three-dimensional (3D) cross-linked polymeric networks capable of retaining substantial amounts of water within their structure. The network formation in hydrogels occurs through either covalent bonds or noncovalent interactions. The noncovalent

interactions primarily include physical entanglements, hydrogen bonding, hydrophobic interactions, supramolecular interactions, electrostatic forces, and coordination interactions, all of which contribute to the mechanical integrity and functional responsiveness of the hydrogel. Both natural polymers (such as polypeptides, polysaccharides, and deoxyribonucleic acid [DNA]) and synthetic polymers (including polyacrylamide and poly(vinyl alcohol)) have been extensively employed in hydrogel synthesis, owing to their tunable physicochemical properties and biocompatibility [4]. Hydrogels are a class of promising biomaterials that have been widely used in the biomedical area. Their uses range from tissue engineering, regenerative medicine, and various therapeutic interventions to the study of physiological and pathological systems. In general, the concentration and composition of the materials, the density and cross-linking techniques, and the construction techniques dictate the characteristics of hydrogel scaffolds as they are created. Colloidal, gelatin, and polyethylene glycol (PEG)-based hydrogels are examples of varied compositions that typically correspond to fibrous, macroporous, and nanoporous architectures, respectively.[4]

Hydrogels are frequently categorized based on their physical characteristics, crosslinking technique, electrical charge of the network, sources, configuration, and polymer composition. Figure 1 summarizes how hydrogels are classified:

For instance, hydrogels can be classified as natural, synthetic, or hybrid based on the source of the polymer network. Copolymeric and multi-polymeric networks are crosslinked in these polymer hydrogels. Chemical and physical hydrogels that are single, double, and multi-polymers are produced by chemically or physically crosslinking the single, double, and multipolymer.

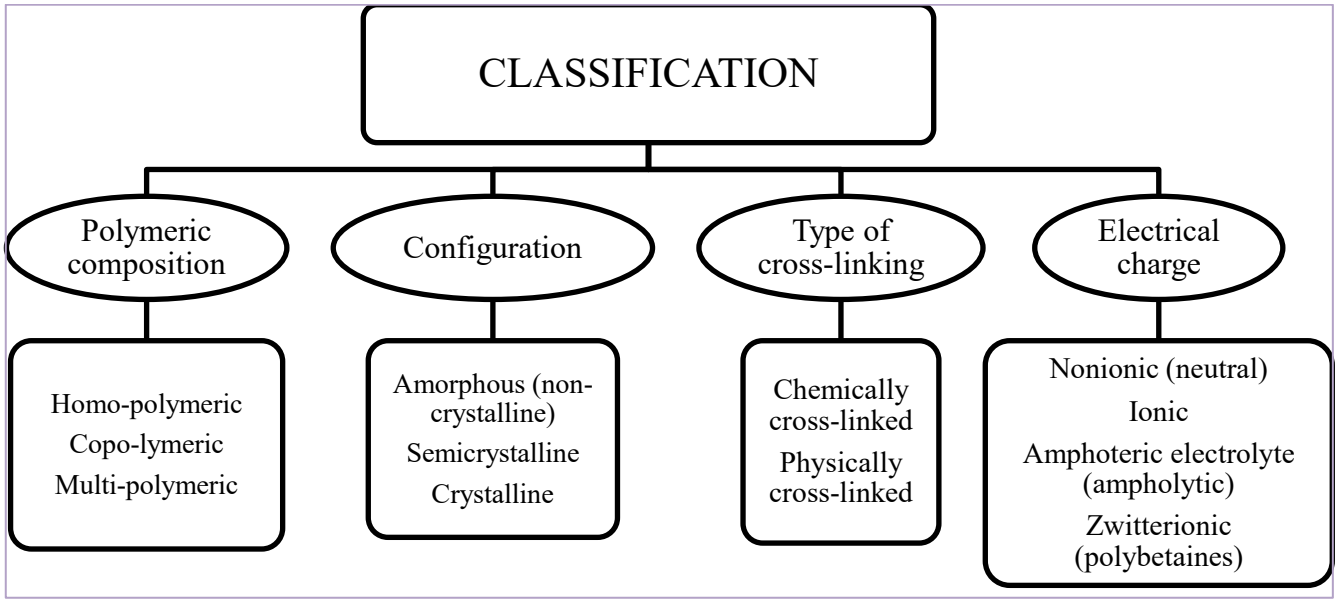

Figure 1: Classification of Hydrogel

Hydrogels can also be classified as crystalline, semicrystalline, or non-crystalline according to their chemical composition, organization, and physical structure. Semicrystalline materials include both crystalline and amorphous components, which is significant.[5]

To create biomaterials that improve or restore tissue function, the multidisciplinary area of tissue engineering (TE) combines the living sciences and engineering. Biocompatible and biodegradable scaffolds are essential components of TE; they are extremely porous three-dimensional structures that promote tissue regeneration, cell proliferation, and differentiation. Cells, growth hormones, or medications are frequently included into these scaffolds to enhance therapeutic results. One of the main goals is to imitate the extracellular matrix (ECM), which gives regeneration biochemical and mechanical cues. Even with TE's promise, there are still issues with processing and material selection. Because of their ECM-like qualities—such as their high water content, flexibility, and biocompatibility—hydrogels have drawn interest and are hence perfect for use in biomedical applications.Hydrogels are presented as a promising solution for a number of well-known potential applications, including wound healing and controlled medication release.[6]

Bioflavonoids are among the many pharmacologically active substances that are known to have strong anti-inflammatory effects. This class of secondary metabolites has a variety of medicinal uses and is obtained from plants. Numerous positive effects are provided by rutin, such as antiviral, antioxidant, neuroprotective, vasoprotective, anti-inflammatory, and anticancer qualities.[7]

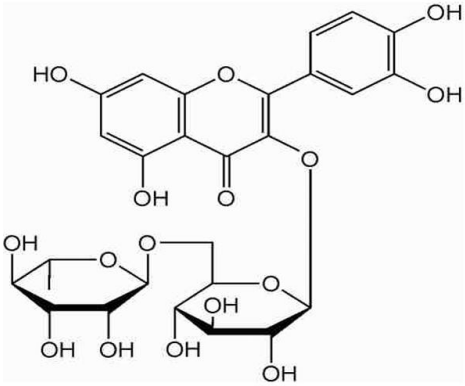

Figure 2: Structure of Rutin Trihydrate

Because of its potent anti-inflammatory properties, rutin trihydrate was chosen as the active ingredient. Its low water solubility (0.125 g/L) presents a major obstacle for topical administration, nevertheless. Hydrogels were used as drug carriers to get around this restriction because of their superior water retention, prolonged release, and skin penetration capabilities, which improved the bioavailability and therapeutic efficacy of rutin trihydrate in dermal applications.[8]

An enhancer can either convey the permeant through the stratum corneum (SC) or change the structure of the SC to make it easier for the permeant molecule to penetrate By demonstrating some kind of boosting action, hundreds of chemical entities have been labeled skin penetration enhancers. Of the different solvents due to their tiny hydrophobic hydrocarbon domains, Transcutols can disrupt the hydrogen bonding network between water molecules. They can also improve penetration and permeation by changing the drug-vehicle characteristics. They can lessen the total intermolecular attraction of water molecules because they have hydrophilic hydrogen-bonding groups (hydroxyl function) that guarantee miscibility with water.Transcutol diffuses into the skin and modifies the permeant's solubility there.

Increased solubilization of a hydrophobic solute is made possible by the reduction of polarity in the aqueous medium caused by the addition of an organic cosolvent that is less polar than water. Rutin exhibit poor solubility in aqueous media but higher solubility in methanol Therefore, methanol was utilized as a cosolvent for rutin to increase its solubility.[14]

Therefore, using various combinations of Transcutol P and Carbopol 934P, the current study attempts to create, develop, and optimize a topical hydrogel drug delivery system incorporating rutin trihydrate. In order to create a stable and efficient hydrogel with desirable properties for topical application, such as suitable consistency, spreadability, and patient acceptability, the work also focuses on optimizing the ratio of Transcutol P and Carbopol 934P. The viscometric and rheological characteristics of the generated hydrogel formulations will be assessed in order to assess how polymer concentration affects the gel's overall consistency and flow behavior. Additionally, by measuring the penetration of rutin trihydrate through the skin at different concentrations of the enhancer, the study aims to explore the function of Transcutol P as a skin-permeability enhancer and determine its efficacy in enhancing transdermal drug delivery.

2. MATERIALS AND METHODS

Rutin trihydrate, Carbopol 934, Transcutol P, triethanolamine, preservatives (methyl and propyl paraben), and analytical-grade reagents were procured from standard suppliers(LobachemPvt. Ltd. and Merck).

Preformulation Studies

a) **Organoleptic Characteristics:**The drug (Rutin) was evaluated for its appearance, color, odor and taste.[15]

b) **Determination of wavelength using UV-visible spectroscopy:** 10 mg rutin trihydrate was weighed and dissolved into 10 ml of methanol to prepare a 1000 ug/ml stock solution from which a 10ug/ml dilution was prepared. Baseline Correction was performed using methanol and then sample was scanned between 200-400 nm and wavelength of maximum absorbance (max) was determined. [12]

c) Calibration curve of Rutin trihydrate:

Preparation of stock solution

Accurately weighed 100mg of rutin trihydrate was transferred into a 100ml volumetric flask & dissolved in Sml of methnol. Then sonicated for 15 minutes and the volume was made up with phosphate buffer pH 6.8 to obtain a 1000pg/ml stock solution of rutin trihydrate and the solution was denoted as "Stock A". From the above Stock A solution, 1ml was pipetted into the 10ml volumetric flask and volume was made up with phosphate buffer pH 6.8 to obtain a 100ug/ml of solution and denoted it as "Stock B".

Preparation of dilution

From Stock B solution the appropriate aliquot of 0.2ml, 0.4ml, 0.6ml, 0.8ml, and 1.0 ml were pipetted into different 10 ml volumetric flask and diluted up to 10ml with phosphate buffer pH 5 to get different concentration range 2-10 ug/ml. The absorbance of each dilution was noted.

Calibration curve of rutin trihydrate in distilled water:

Preparation of stock solution

Accurately weighed 100mg of rutin trihydarte was transferred into a 100ml volumetric flask & dissolved in Sml of. Then sonicated for 15 minutes and the volume was made up with distilled water to obtain a 1000ug/ml stock solution of rutin trihydarte and the solution was denoted as "Stock A". From the above Stock A" solution, 1ml was pipetted into the 10ml volumetric flask and volume was made up with distilled water to obtain a 100ug/ml of solution and denoted it as "Stock B"

Preparation of dilution

From Stock B solution the appropriate aliquot of 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml and 1.0 ml were taken into different 10 ml volumetric flask and diluted up to 10ml with distilled water to get different concentration range 2-10 ug/ml. The absorbance of each dilution was noted.

d) Determination of solubility of Rutin tryhydrate in various mediums:

The solubility of Rutin trihydrate in various medium was determined by shake flask method. 5ml of each solvent was taken into a vial and an excess amount of Rutin trihydrate was added. After solubilization of Rutin trihydrate, an extra amount of Rutin trihydrate was added to the vials and stirred for a period of 6 hours (saturation time). The process was repeated until saturation solubility of Rutin trihydrate, indicated by presence of undissolved drug. The mixtures were then kept at room temperature for 24 hrs. and the solution were filtered through whatman filter paper. Then diluted with respective solvents i.e phosphate pH buffer 6.8 and pH 5.0, methanol, and distilled water.The drug concentration was analyzed spectrophotometrically at 241.50nm by using UV-visible spectrophotometer (Shimadzu-1800)[16,17]

d) Drug-excipient interaction study:

The compatibility of the drug was assessed by drug-excipient interaction study. The drug was mixed with various excipients in a 1:1 ratio in glass vials which were properly sealed &labeled and kept undisturbed at 50°C temperature and 75% RH for 15 days. Physical and chemical observations of all the mixtures were done on initial day and 15th day by TLC.[18]

Thin layer chromatography:

Preparation of TLC Plates:

Firstly silica gel-G slurry prepared by mixing silica gel-G with distilled water in mortar pestle and triturated continuously to make uniform slurry. The glass slide was taken, and the slurry was poured uniformly on the glass slide and allowed to dry TLC plate was placed in a hot air oven at 120 °C for activation.

Preparation of sample: Each chemical was sufficiently dissolved in pure methanol. The material was spotted on TLC plates using a capillary tube. Each spot's diameter was restricted to 0.3 cm. At 1 cm intervals from the plate's bottom, the compounds were spotted. Let it air dry. The solvent system's development: Ethyl acetate: glacial acetic acid: H,0 (7.5:1.5:1.5) was utilized as the mobile phase to create the solvent system. They utilized a 100 ml tiny beaker and filled it with the solvent system. Filter paper was used to line the glass beaker so that the solvent system could pre-saturate it for 15 to 30 minutes.

Stationary phase - Pre coated silica gel plate

Mobile phase - Ethyl acetate: glacial acetic acid: H,0(7.5:1.5:1.5)

Development of thin layer plate:

Plates were developed in an ascending manner. When the solvent reached to the mark the plate was removed and the wet plates were dried.

Detection of spot:

The iodine chamber was prepared and TLC plate was placed in a chamber. Thereafter the plate was removed from chamber and spot was observed.

Calculation of Rf value:

Rf value can be calculated by following formula:

Rf= Distance travelled by solute/ Distance travelled by solvent

Preparation of Hydrogel

Carbopol 934 was dispersed in water and allowed to hydrate for 24 hours. Themethanolic dispersion of rutin (1mg/ml) was added to Transcutol P, then incorporated into the hydrated Carbopol dispersion. The formulation was neutralized with triethanolamine to adjust pH and achieve gel consistency. Preservatives were incorporated, and gels were equilibrated for 24 hours before evaluation.

Table 1: Composition of various Hydrogel formulations

S.N.	Ingredients	FD1 (mg)	FD2 (mg)	FD3 (mg)	FD4 (mg)	FD5 (mg)	FD6 (mg)	FD7 (mg)	FD8 (mg)	FD9 (mg)
1	Drug (rutin trihydrate)	5	5	5	5	5	5	5	5	5
2	Carbopol 934	0.5	0.5	0.5	1	1	1	1.5	1.5	1.5
3	Transcutol P (in ml)	5	10	15	5	10	15	5	10	15
4	Methyl paraben	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
5	Propyl paraben	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
6	Triethnolamine (TEA) (ml)	qs	qs	qs	qs	qs	qs	qs	qs	qs
7	Water	Qs 100gm	Qs 100gm	Qs 100gm	Qs 100gm	Qs 100gm	Qs 100gm	Qs 100gm	Qs 100gm	Qs 100gm

Evaluation of Hydrogel

Physical appearance & Homogenecity: Visual inspection was used to assess the appearance of each hydrogel formulation. On the other hand, homogeneity was assessed by separating the little amounts of hydrogel formulations between the thumb and index finger and looking for any coarse particles. In a similar manner, a tiny quantity of hydrogel compositions was put to the hand's back and rubbed separately. For every formulation, the identical process was carried out three times, and the results are listed in a table.

Washablity: After applying the formulations to the skin, the degree and ease of washing with water were manually assessed. Results were listed in table 5.

Examining extrudability: The hydrogel formulations were put inside aluminum or metal tubes that could be folded. After pressing the tubes to extrude the material, the formulation's extrudability was examined.[11]

pH Measurement: The pH of each hydrogel composition was measured with a digital pH meter. Distilled water was used to dissolve 1.0 g of each hydrogel, which was then kept at room temperature for two hours. After that, the pH was measured in triplicate and the average was determined. These figures were tallied in Table6.

Viscosity: A Brookfield viscometer was used to conduct a rheological analysis of every gel. The gel-filled Brookfield digital viscometer was placed within the viscometer's flow jacket. The viscosity of gel formulations was measured using a sample adapter rotating at a speed of 20 rpm. The water on the thermostated water jacket was rotated to maintain the temperature at 25°C. Before the six-minute mark, the sample was settled. By raising the sharing rate value, the viscosity of all hydrogels can be determined.

Spreadability: The spreading area of 1.0 g hydrogel between two glass slides with diameters of 20 cm by 20 cm was measured to determine spreadability. To test the spread ability, a typical weight of approximately 125+1 g was placed on the upper slide for 60 seconds. The following formula was used to compute the dispersed gel's diameter, which was measured in centimeters. The results are given in table

$$S = \frac{MxL}{T}$$

In this case, L = length in centimeters moved on the glass slide, T = time in seconds, and M = weight (g) placed on the upper glass slide.[9]

Drug Content: The technique used to extract the drug from the formulations determined the drug content of the generated gel formulations. A 1g formulation was sonicated at 125 W for 30 minutes in 20 ml of phosphate buffer (pH 6.8) Membrane filter 0.45 um was then used to filter the mixture. Spectrophotometry at 255.5nm (Shimardzu 1800 UV-VIS spectrophotometer)was used to evaluate the drug content). The concentration of Rutin Trihydrate was estimated from the calibration curve.[10]

In vitro Release Studies: The produced hydrogel's in vitro drug release was assessed. Using a cellophane membrane(soaked in pH 6.8 for two hours before use), an in vitrodiffusion research was conducted in a Franz diffusion cell (with effective diffusion area 3.14 cm and 15.5 ml cell volume). The Franz diffusion cell was equipped with a cellophane membrane. The formulation was administered to the dialysis membrane via the donor compartment. The reservoir compartment was filled with 25 milliliters of pH 6.8 phosphate buffer. The investigation was conducted for four hours at 37 ± 1°C and 100 rpm. Samples were taken out of the reservoir compartment every 30 minutes, and absorbance at 255.5 nm was recorded using spectrophotometry. The reservoir compartment was filled with an identical amount of 6.8 pH phosphate buffer each time.[11]

3. RESULTS AND DISCUSSION:

Using a concentration of 10µg/ml in methanol, the drug solution's spectra was analyzed in a double beam ultraviolet spectrophotometer to determine the absorption maxima of rutin trihydrate. In methanol, phosphate buffers (pH 5.0, 6.8), and distilled water, rutin trihydrate exhibited a linear relationship with a correlation coefficient of 0.999 in the concentration range of 2-10µg/ml (Figure 1). The drug's melting point was discovered to be between 198±2°C. The preformulation study's data were all determined to be consistent with the standard monograph, confirming the drug's authenticity and purity and allowing it to be employed in the development of a rutin-loaded hydrogel formulation. Rutin had low solubility in aqueous medium but increased solubility in methanol, suggesting the use of cosolvent systems for hydrogel formation. TLC analysis confirmed that rutin and excipients did not significantly interact after quick stability testing.

Determination of λmax: The maximum wavelength of Rutin trihydrate was found to be 255.5+2nm.

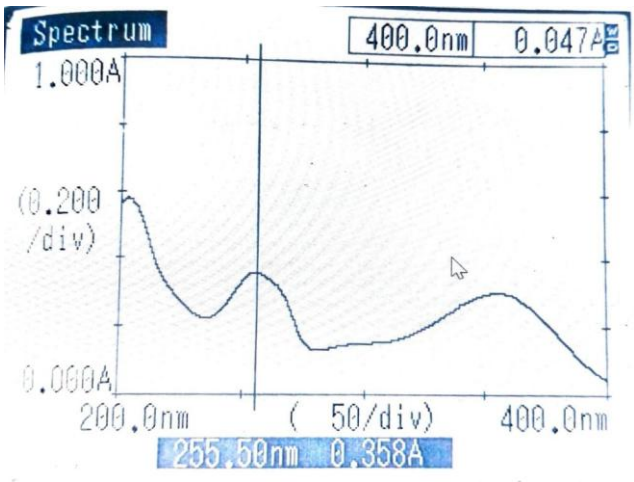

Figure 3: Absorbance Maxima of Rutin Trihydtrate

Preparation of calibration curve of Rutin trihydrate:

Calibration curve of Rutin trihydrate in methanol: The calibration curves of Rutin trihydrate in methanol were prepared and shown below:

Table 2: Absorbance data of Rutin trihydrate in Methanol

Sno.	Concentration(ug/ml)	Absorbance (mean ± standard deviation) (n=3)
1	2	0.082+0.003
2	4	0.161+0.004
3	6	0.227+0.003
4	8	0.295+0.002
5	10	0.370+0.005

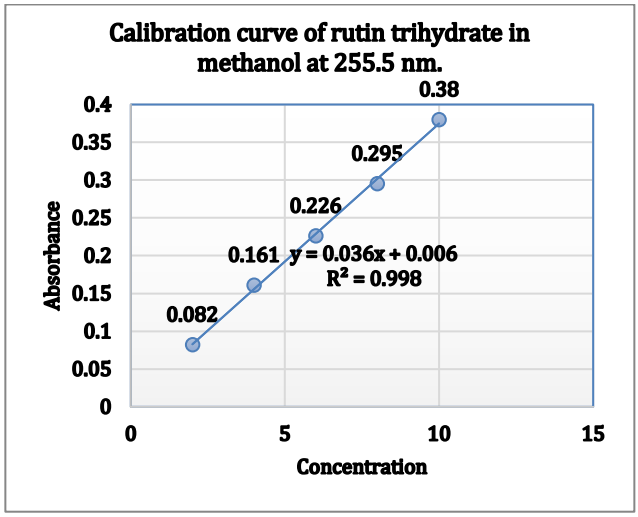

Figure 4: Calibration graph of Rutin Trihydrate in Methanol

Rutin trihydrate in Methanol follows the Beer - Lambert's law in the concentration range of 2-10 mg/ml.

Calibration curve of Rutin trihydrate in phosphate buffer pH 6.8: The calibration curves of Rutin trihydrate in phosphate buffer pH 6.8 were prepared and shown below:

Table 3: Absorbance data of Rutin trihydrate in phosphate buffer pH 6.8.

Sno.	Concentration (ug/ml)	Absorbance (mean ± standard deviation) (n=3)
1	2	0.078+0.003
2	4	0.161+0.004
3	6	0.229+0.003
4	8	0.308+0.004
5	10	0.384+0.004

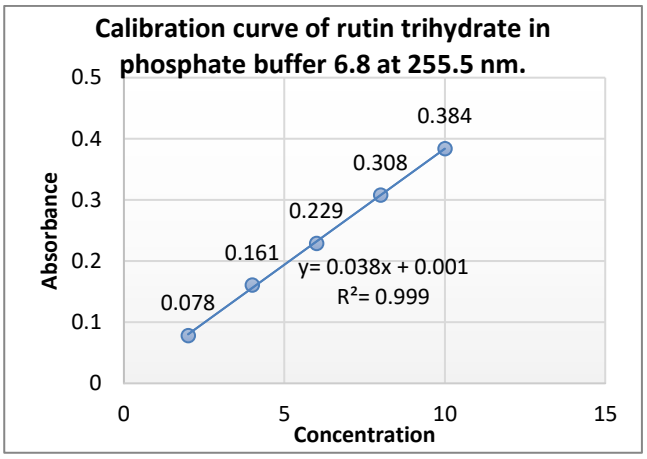

Figure 5: Calibration graph of Rutin Trihydrate in pH 6.8

Rutin trihydrate in phosphate buffer pH 6.8 follows the Beer-Lambert's law in the concentration range of 2-10 ug/ml.

Calibration curve of Rutin trihydrate in phosphate buffer pH 5.0: The calibration curves of Rutin trihydrate in pH 1.2 HCI buffer were prepared and shown below:

Table 4: Absorbance data of Rutin trihydrate in Phosphate buffer pH 5.0

Sno.	Concentration (ug/ml)	Absorbance (mean ± standard deviation) (n=3)
1	2	0.052+0.001
2	4	0.112+0.002
3	6	0.17+0.002
4	8	0.225+0,003
5	10	0.263+0.001

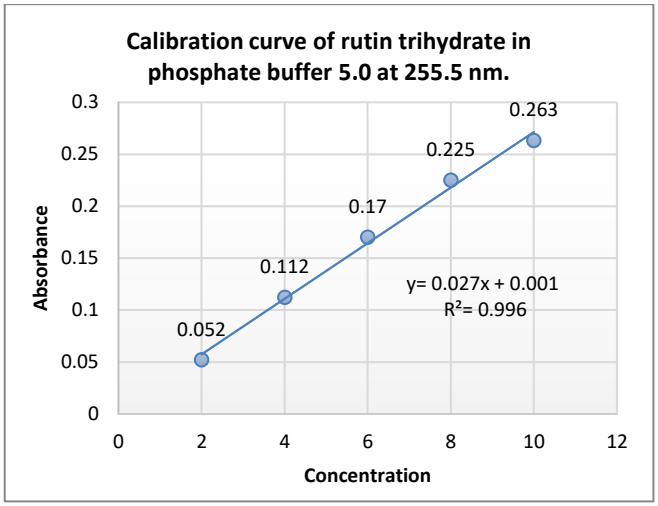

Figure 6: Calibration graph of Rutin Trihydrate in Phosphate buffer pH 5.0

Rutin trihydrate in phosphate buffer pH 5.0 follows the Beer-Lambert's law in the concentration range of 2-10 ug/ml.

Calibration curve of Rutin trihydrate in water:

The calibration curves of Rutin trihydrate in water were prepared and shown below:

Table 5: Absorbance data of Rutin trihydrate in water.

Sno.	Concentration (ug/ml)	Absorbance (mean ± standard deviation) (n=3)
1	2	0.071±0.002
2	4	0.13+0.002
3	6	0.186+0.003
4	8	0.252+0.003
5	10	0.305+0.004

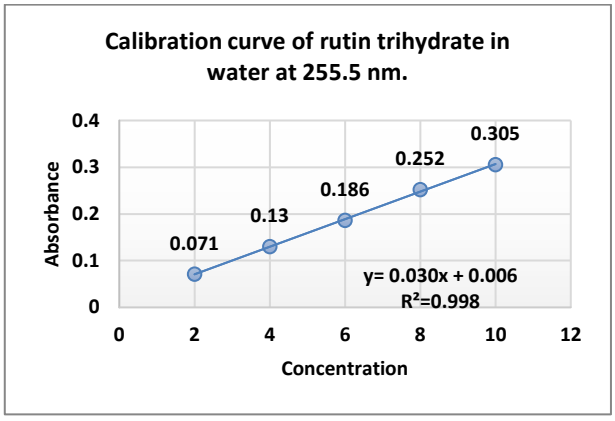

Figure 7: Calibration graph of Rutin trihydrate in water

Rutin trihydrate in water follows the Beer -Lambert's law in the concentration range of 2-10 ug/ml

Calibration curve of Rutin trihydrate in Transcutol P.

The calibration curves of Rutin trihydrate in propylene glycol were prepared and shown below:

Table 6: Absorbance data of Rutin trihydrate in Transcutol P

Sno.	Concentration (ug/ml)	Absorbance (mean ± standard deviation) (n=3)
1	2	0.095+0.003
2	4	0.202+0.003
3	6	0.312+0.003
4	8	0.418+0.003
5	10	0.535+0.003

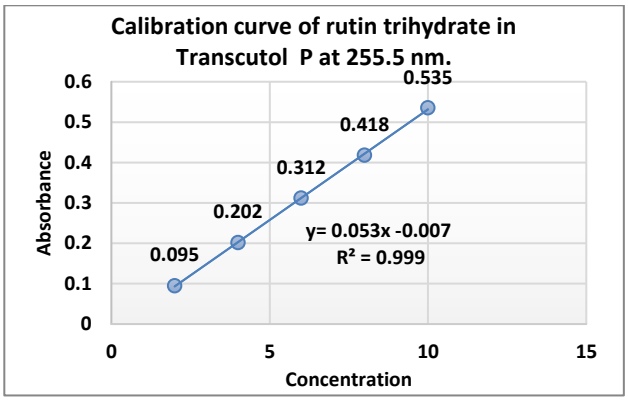

Figure 8 Calibration graph of Rutin trihydrate in Transcutol P

Rutin trihydrate in Transcutol P follows the Beer Lambert's law in the concentration range of 2-10 g/ml.

Determination of solubility of Rutin trihydrate in various medium:

Table 7: Solubility data of Rutin trihydrate in different mediums

SNo.	Solvent	Solubility (mg/ml) Mean+SD (=3)	Inference
1	Methanol	104.99±2.1 72	Freely soluble
2	Phosphate buffer pH 5.0	0.008±0.0005	Practically insoluble
3	Phosphate buffer pH 6.8	0.022±0.0005	Practically insoluble
4	Distilled water	0.256±0.001	Very slightly soluble
5	Transcutol P	21.94±1.28	Sparingly soluble

Discussion: Rutin trihydrate showed wide variability in solubility across tested media: it was freely soluble in methanol (104.99 ± 2.17 mg/mL), sparingly soluble in Transcutol P (21.94 ± 1.28 mg/mL), very slightly soluble in distilled water (0.256 ± 0.001 mg/mL), and practically insoluble in phosphate buffers pH 5.0 (0.008 ± 0.0005 mg/mL) and pH 6.8 (0.022 ± 0.0005 mg/mL). These results indicate poor aqueous solubility under physiological pH but good solubility in organic solvents and solubilizers, implying that co-solvents or formulation strategies (e.g solid dispersions, lipid systems, or nanocarriers) will be necessary to improve rutin's dissolution and bioavailability.

Cosolvency for Solubility Enhancement: Cosolvent techniques make weakly water-soluble medications seem more soluble by using water-miscible organic solvents. They are frequently used with other methods like cyclodextrins or surfactants in oral and parenteral formulations.

Enhancement of Solubility

Cosolvents, such as ethanol, methanol, propylene glycol, PEG 400, and glycerin, increase solubility by reducing solvent polarity and upsetting the hydrogen-bond network in water, which lessens the solvent's propensity to "squeeze out" hydrophobic solutes.

Cosolvent Systems to Improve Rutin Solubility

Cosolvent-type systems can boost rutin's solubility by tens to hundreds of times, but "advanced" cosolvents like methanol–water or natural deep eutectic solvents (NADES) are frequently the most effective.

Rutin solubility in water-methanol mixtures (up to 0.1 mole fraction methanol) increased with increasing methanol level at 25 °C.

Methanol produces classic cosolvencybehavior by reducing the polarity of water and better solvating the hydrophobic, aromatic portions of rutin.

Drug-excipient interaction study:

The compatibility was assessed by TLC and the retention factors of all ratios found similar.

Table 8: Data of drug-excipient interaction study

S.N.	Drug/ drug+ Excipient Ratio (1:1)	Physical appearance (initial)	Present Day (Rf)	Physical appearance (final)	After 15 days (Rf)	Inference
1	Drug (Rutin trihydrate)	Yellow	0.45	White	0.45	No Change
2	Pure Drug + cabopol 934	Whitish yellow	0.46	Whitish yellow	0.45	No Change
3	Pure Drug + Transcutol P	Yellowish Transparent	0.44	Yellowish Transparent	0.44	No Change
4	Pure Drug + Methyl paraben	Whitish yellow	0.45	Whitish yellow	0.44	No Change
5	Pure Drug + Propyl peraben	Whitish yellow	0.44	Whitish yellow	0.45	No Change

Discussion: The drug–excipient compatibility study of Rutin trihydrate (1:1 ratios) showed no evidence of interaction: the pure drug remained yellow with Rf 0.45 (unchanged after 15 days despite a change in surface appearance to white), and mixtures with Carbopol 934 (Rf 0.46 → 0.45), propylene glycol (0.44 → 0.44), methyl paraben (0.45 → 0.44) and propyl paraben (0.44 → 0.45) exhibited only negligible Rf shifts (±0.01) and no meaningful physical changes. These minor variations are within experimental error, so all tested excipients are considered compatible with rutin trihydrate under the study conditions.

Physical appearance &Homogenecity:

Table 9: Formulation batches' physical parameters

Formulation	Homogeneity	Appearance	Consistency
FD1	Very Good	Whitish yellow	Medium-soft hydrogel
FD2	Very Good	Whitish yellow	Medium-soft hydrogel
FD3	Very Good	Whitish yellow	Medium-soft hydrogel
FD4	Excellent	Whitish yellow	smooth & spreadable
FD5	Excellent	Whitish yellow	smooth & spreadable
FD6	Excellent	Whitish yellow	smooth & spreadable
FD7	Good	Whitish yellow	Thick, highly viscous gel
FD8	Good	Whitish yellow	Thick, highly viscous gel
FD9	Good	Whitish yellow	Thick, highly viscous gel

Washability, Extrudability, And Spreadability

Table 10: Findings from the study on washability, extrudability, and Spreadability

Formulation	Washability	Extrudability	Spreadability (cm)
FD1	Excellent	Very Good	63.66+1.52
FD2	Excellent	Good	61.46+1.11
FD3	Very Good	Very Good	61.9+1.6
FD4	Excellent	Excellent	58.33+1.52
FD5	Excellent	Excellent	58.33+1.48
FD6	Very Good	Excellent	59.26+0.84
FD7	Average	Average	54.3+0.85
FD8	Good	Poor	54.6+1.22
FD9	Average	Average	52.83+1.13

Discussion: Hydrogel formulations were white viscous creamy preparation with a smooth homogeneous texture and glossy appearance. Results have been discussed in Table 11.

The results of washability, extrudability and spreadability of all formulation were given in Table 3. From the result it was found that formulation F1-F5 has good washability ability, formulation F2, F3 has good Extrudability and Spreadability of all formulation was found to in range of 12.25-14.56.

Table 11: Result of viscosity, pH and drug content

Formulation	pH	Viscosity (cP)	Drug Content (%)
FD1	7.07+0.03	8785.33±2.51	99.02+0.558
FD2	7.17+0.04	8757.33±8.73	97.71+0.101
FD3	7.19+0.01	8882.33±2.51	97.75+0.036
FD4	7.12+0.02	12522.33±2.51	98.85+0.08
FD5	7.18+0.01	12154.33±4.04	97.77+0.,04
FD6	7.11+0.06	12183.33±4.16	97.24+0.402
FD7	7.11+0.01	15959.66±8.73	96.71+0.401
FD8	6.8+0.16	15959.66±8.73	96.48+0.579
FD9	7.14+0.02	15927.25±6.24	98.93+0.035

Viscosity:

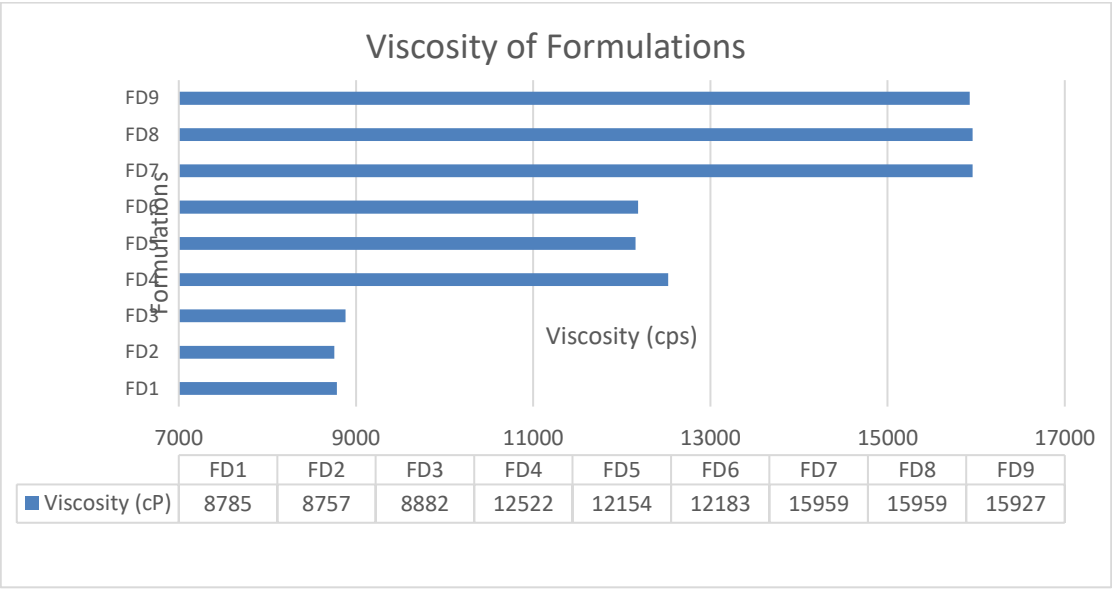

Figure 9 Rheological study data

Discussion: From FD1 to FD9, viscosity values gradually increased, ranging from 8757.33 ± 2.51 cP to 15959.66 ± 8.73 cP. Higher viscosity formulations (FD7–FD9) produced thicker, more structured gels, while lower viscosity formulations (FD1–FD3) showed superior flow characteristics.

Higher polymer concentrations and more robust cross-linking within the gel matrix, which improves gel strength and structural integrity, are responsible for the rise in viscosity. To guarantee appropriate spreadability, retention at the application site, and controlled medication release, enough viscosity is necessary. However, an ideal balance is needed because an excessively high viscosity may make application more difficult.

Spreadability: Transcutol P increased, spreadability improved because of the corresponding decrease in viscosity. Formulations FD1–FD3 showed higher spreadability, however a progressive decline was shown as viscosity increased. The formulation with the least spreadability was FD9**.**

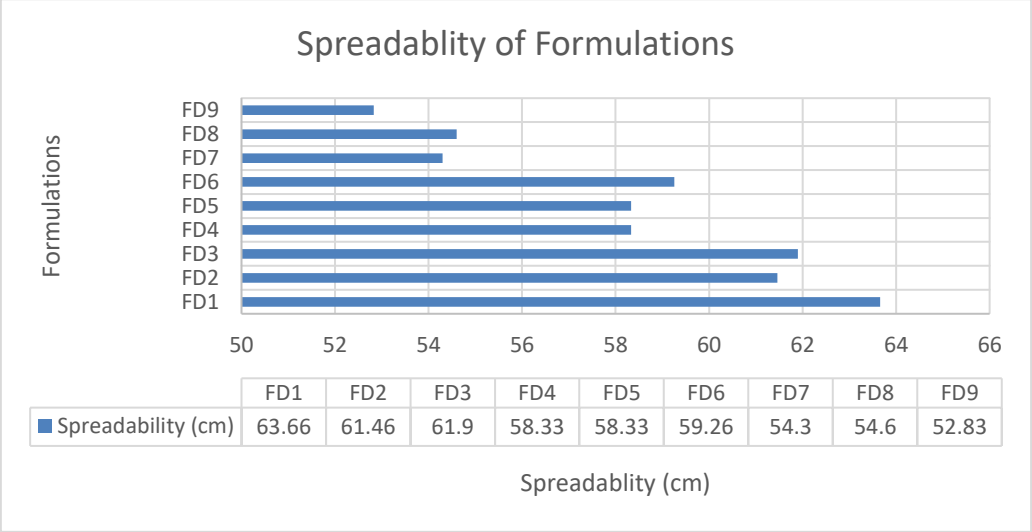

Figure 10: Spreadablity Study Data

Discussion: The values of spreadability varied between 52.83 ± 1.13 cm and 63.66 ± 1.52 cm. Spreadability was higher for formulations FD1, FD2, and FD3, suggesting that they were easier to apply to the skin's surface. Moderate spreadability, which is thought to be perfect for topical hydrogels because it permits sufficient coverage without excessive flow, was demonstrated by formulationsFD4–FD6.

FD7, FD8, and FD9 had lower spreadability ratings, which could be explained by their higher viscosity, which makes spreading more difficult. In hydrogel systems, it is frequently observed that spreadability decreases as polymer concentration rises.

pH :

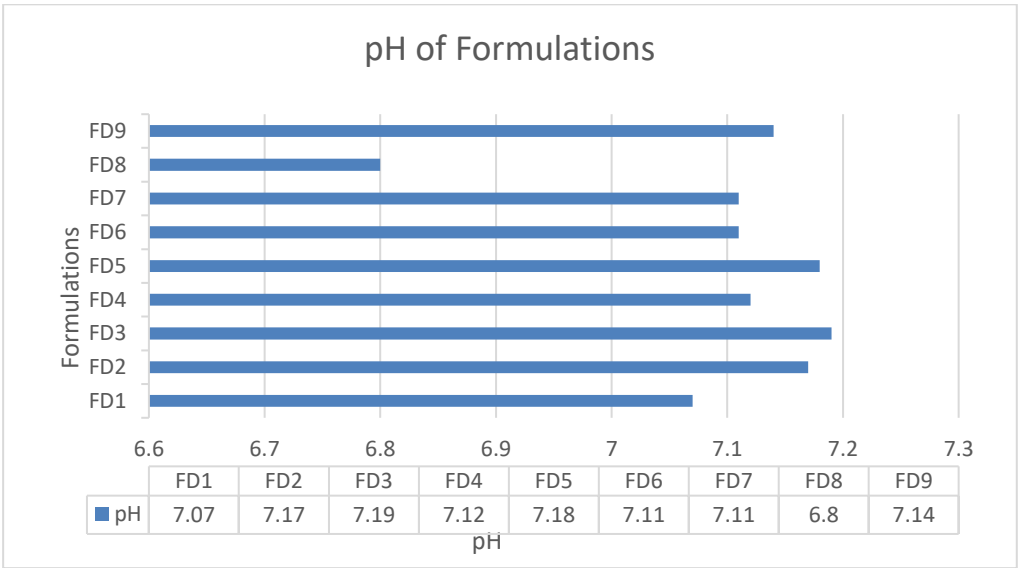

Figure 11: pH study Data

Discussion: All formulations had pH values between 6.8 ± 0.16 and 7.19 ± 0.01, which showed that the hydrogels were skin-compatible and almost neutral. For topical treatment, this pH range is ideal since it reduces the possibility of skin irritation and discomfort. fluctuations in polymer concentration and formulation makeup may be the cause of slight pH fluctuations between formulations. Overall, the pH values indicate that the produced hydrogels have acceptable physiological acceptability.

Content of Drugs:

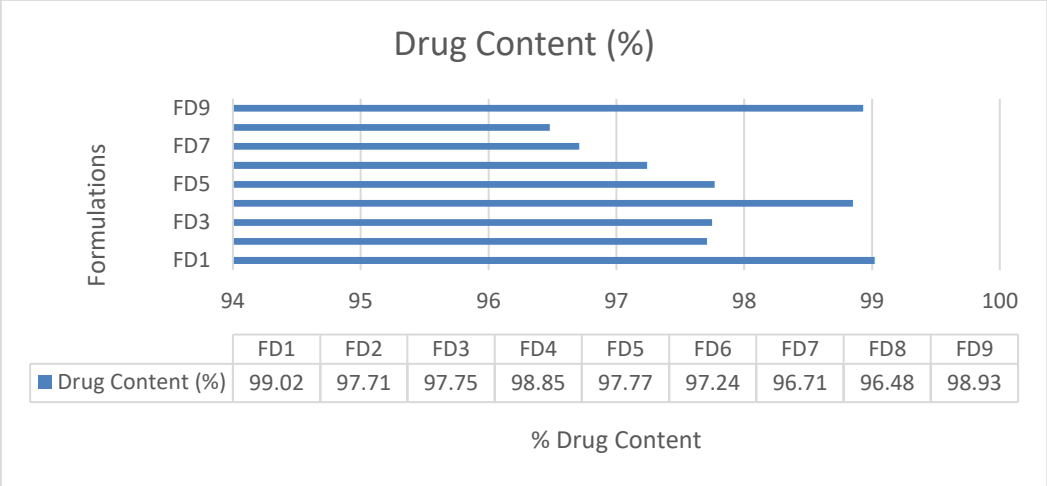

Figure 12: Drug content study

Discussion: The drug content was consistent across the hydrogel matrix, ranging from 96.48 ± 0.579% to 99.02 ± 0.558% in all formulations. This shows good mixing and no medication deterioration during the formulation process. All readings were within pharmacopeial acceptable limits (95–105%), while formulation FD1 had the highest drug content (99.02%) and FD8 had the lowest (96.48%).

- **In Vitro Release:**

Table 12: Percentage cumulative drug release data of Fl to F9 formulation of Hydrogel

Time (in hrs)	**% Cumulative drug Release (Mean±SD)**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0.5	12.66 ±1.7	13.46 ±0.70	15.93± 0.40	14.11± 0.67	11.20 ±0.5	13.24 ±0.6	9.96 ±0.25	13.06 ±0.8	11.53 ±0.55
1	27.01 ±3.36	31.34±1.26	30.93 ±0.4	32.22 ±1.95	20.83±0.56	31.25 ±1.3	21.5±0.52	32.36 ±1.2	22.00 ±1.00
2	48.46 ±0.9	40.52 ±1.31	39.8 ±0.65	41.13 ±0.66	34.5 ±0.65	40.43 ±0.92	34.96 ±1.05	41.13 ±0.8	38.32 ±0.54
3	58.96 ±4.09	53.68 ±1.32	54.5 ±0.81	53.41 ±0.95	52.53 ±0.5	53.33 ±1.18	52.6 ±0.52	53.24±0.8	54.16 ±1.15
4	61.27 ±1.05	61.48 ±1.32	61.53 ±0.55	65.35 ±1.34	62.73 ±0.7	65.52 ±0.94	61.33 ±0.76	65.96 ±0.8	64.03 ±0.95
5	71.25 ±0.75	70.69 ±1.18	68.5 ±0.5	68.85 ±0.66	71.5 ±0.65	67.54 ±0.65	70.73 ±0.75	67.62 ±0.52	72.30 ±0.8
6	83.03±1.98	77.44±1.32	73.86 ±0.85	73.33 ±1.33	73.26 ±0.83	72.19 ±0.40	73.26 ±0.83	71.82 ±1.03	78.9 ±0.80
7	99 ±0.63	90.52 ±1.31	90.56 ±0.50	81.92 ±0.66	79.26 ±0.9	81.22 ±0.66	80.9 ±0.65	81.35 ±0.6	87.90 ±1.55

Discussion: Controlled diffusion from the hydrogel matrix was indicated by the time-dependent rise in cumulative drug release over 7hrs in the in vitro drug release profiles of formulations F1–F9. Effective drug trapping inside the polymeric network was suggested by the steady and continuous release that followed the initial release of 9.96–15.93% at 30 minutes, which was attributed to surface-associated drug.

Cumulative drug release increased to 67.54–72.30% after 5hrs from 52.53% to 58.96% at 3hrs, indicating diffusion-controlled drug transport made possible by polymer swelling. F1 demonstrated the largest drug release (99.00 ± 0.63%) after 7hrs, although F2, F3, and F9 showed releases greater than 87%. Formulations F4–F8 showed comparatively slower release (79.26–81.92%), perhaps as a result of higher diffusional resistance and viscosity.

Overall, polymer content and viscosity had a significant impact on drug release; formulations with lower to moderate viscosity allowed for rapid diffusion, while formulations with high viscosity allowed for prolonged release. This suggests that the created hydrogels are suitable for topical drug administration.

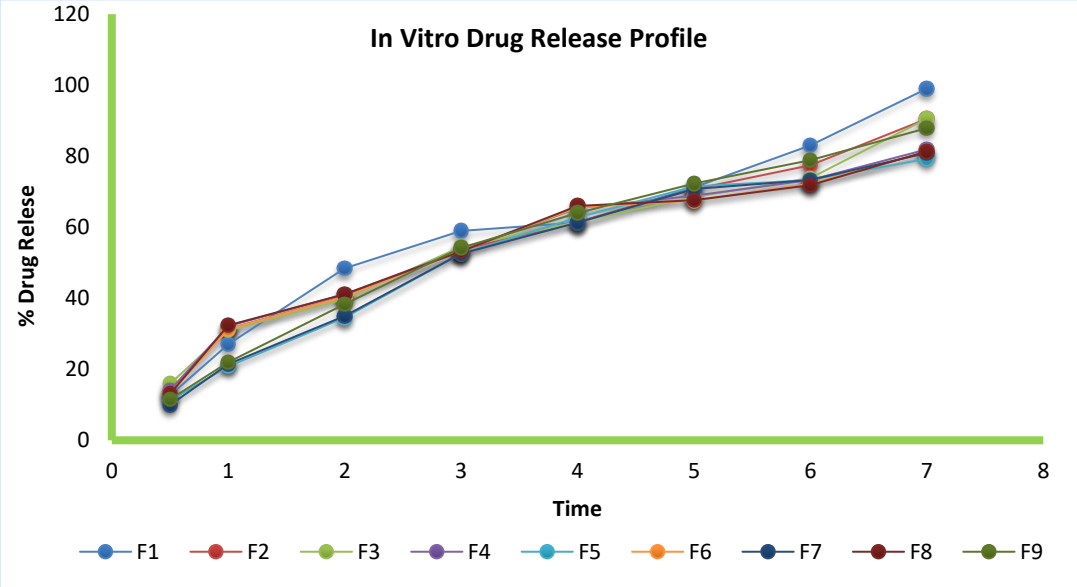

Figure 13: In vitro drug release

4. CONCLUSION:

A number of topical hydrogel formulations were effectively created and assessed in this work, which also methodically examined their physicochemical parameters, application features, and in vitro drug release behavior. Formulation stability and topical administration compatibility were confirmed by the skin-compatible pH, adequate viscosity, and consistent drug content displayed by all formulations.

Evaluation metrics like spreadability, extrudability, and washability shown a significant correlation with gel viscosity. While extremely viscous formulations had degraded application qualities and delayed drug diffusion, lesser viscosity formulations demonstrated greater spreadability and faster drug release. Moderately viscous hydrogels struck the ideal balance between application ease and adequate retention at the application site.

For all formulations, in vitro drug release experiments showed a regulated and sustained release profile over a 7hrs period. The release behavior showed a strong correlation with polymer concentration and formulation viscosity, suggesting a diffusion-controlled mechanism of drug release from the hydrogel matrix. Lower viscosity formulations showed faster drug release, but excessively viscous formulations showed slower release because of greater diffusionalresistance. Among the tested formulations, 5% TranscutolP provided the best balance between enhancing drug permeation and maintaining favorable formulation characteristics.

Overall, carbopol proved to be an effective gelling agent for rutin trihydrate gel formulations, while Transcutol P at optimized concentration enhanced drug release. The results confirmthat both polymer concentration and penetration enhancer levels must be carefully optimized to achieve desired therapeutic outcomes in topical gel formulations.

REFERENCES:

1. Sharma D, Upadhyay S, Upadhyay P. Rutin trihydrate loaded liposomal gel formulation and characterization. International Journal of Pharmaceutical Research (09752366). 2021 Jan 1;13(1). https://doi.org/10.31838/ijpr/2021.13.01.345

2. Deore UV, Mahajan HS. Hydrogel for topical drug delivery based on Mimosa pudica seed mucilage: Development and characterization. Sustainable Chemistry and Pharmacy. 2022 Jun 1;27:100701. https://doi.org/10.1016/j.scp.2022.100701

3. Sánchez-Cid P, Jiménez-Rosado M, Romero A, Pérez-Puyana V. Novel trends in hydrogel development for biomedical applications: A review. Polymers. 2022 Jul 26;14(15):3023. https://doi.org/10.3390/polym14153023 PMid:35893984 PMCid:PMC9370620

4. Yang D. Recent advances in hydrogels. Chemistry of Materials. 2022 Mar 8;34(5):1987-9. https://doi.org/10.1021/acs.chemmater.2c00188

5. Cao H, Duan L, Zhang Y, Cao J, Zhang K. Current hydrogel advances in physicochemical and biological response-driven biomedical application diversity. Signal transduction and targeted therapy. 2021 Dec 16;6(1):426. https://doi.org/10.1038/s41392-021-00830-x PMid:34916490 PMCid:PMC8674418

6. El Sayed MM. Production of polymer hydrogel composites and their applications. Journal of Polymers and the Environment. 2023 Jul;31(7):2855-79. https://doi.org/10.1007/s10924-023-02796-z

7. Li B, Yang X. Rutin-loaded cellulose acetate/poly (ethylene oxide) fiber membrane fabricated by electrospinning: A bioactive material. Materials Science and Engineering: C. 2020 Apr 1;109:110601. https://doi.org/10.1016/j.msec.2019.110601 PMid:32228961

8. Varshneya AP, Ravikumar P. Formulation and Characterization of Rutin trihydrate liposomes for Topical Delivery. Internaional Journal of Pharmaceutical Research. 2015 Jan.

9. Abbas K, Amin A, Mudassir J, Abdullah Alzahrani AY, Saher T, Manzoor R, Aleem A, Khan MA, Wazir MA, Rana SJ, Abdul khaliq H. Preparation, characterization and evaluation of hydrogels from different fractions of diverse medicinal plants for management of pain and inflammation. International Journal of Food Properties. 2023 Sep 22;26(1):2532-52. https://doi.org/10.1080/10942912.2023.2250572

10. Yen WF, Basri M, Ahmad M, Ismail M. Research Article Formulation and Evaluation of Galantamine Gel as Drug Reservoir in Transdermal Patch Delivery System.

11. Singh V, Chaubey N. Design and evaluation of topical hydrogel formulation of aceclofenac for improved therapy. J. Drug Deliv. Ther. 2019 Sep 1;9:118-22. https://doi.org/10.22270/jddt.v9i5.3605

12. Halagali P, Wannur VI, Patil AK, Torgal VD, Naik SM, Marennavar SA, Shahapurmath S, Patil P. Formulation and evaluation of quercetin ethosomal hydrogel for topical delivery system. Int. J. Pharm. Investig.. 2024 Jul 1;14(3):749-58. https://doi.org/10.5530/ijpi.14.3.84

13. Moldovan OL, Brihan DN, Todoran N, Rusu A. Thin layer chromatographic compatibility study in preformulation of new transdermal therapeutic systems. Acta Marisiensis. Seria Medica. 2020 Mar 1;66(1). https://doi.org/10.2478/amma-2020-0004

14. Musakhanian J, Osborne DW, Rodier JD. Skin penetration and permeation properties of Transcutol® in complex formulations. AAPS PharmSciTech. 2024 Sep 5;25(7):201. https://doi.org/10.1208/s12249-024-02886-8 PMid:39235493

15. Morariu-Briciu DM, Bolintineanu SL, Rata A, Semenescu AD, Anton A, Jijie R, Kis A, Hrubaru I, Heghes A. Assessment of the biosafety profile of Galium verum in vitro on myoblasts and in ovo on chorioallantoic membrane. World Journal of Cardiology. 2025 Feb 26;17(2):102310. https://doi.org/10.4330/wjc.v17.i2.102310 PMid:40061279 PMCid:PMC11886392

16. Zi J, Peng B, Yan W. Solubilities of rutin in eight solvents at T= 283.15, 298.15, 313.15, 323.15, and 333.15 K. Fluid Phase Equilibria. 2007 Dec 1;261(1-2):111-4. https://doi.org/10.1016/j.fluid.2007.07.030

17. Censi R, Martena V, Hoti E, Malaj L, Di Martino P. Permeation and skin retention of quercetin from microemulsions containing Transcutol® P. Drug development and industrial pharmacy. 2012 Sep 1;38(9):1128-33. https://doi.org/10.3109/03639045.2011.641564 PMid:22188183

18. Patel P, Ahir K, Patel V, Manani L, Patel C. Drug-Excipient compatibility studies: First step for dosage form development. Pharma Innov. 2015 Jul 1;4(5):14.