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Formulation and Evaluation of Capsaicin Emulgel for Rheumatoid Arthritis Management

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ABSTRACT:
The present study focuses on the formulation and evaluation of a topical drug delivery system for capsaicin in the form of an emulgel. The emulgel was developed using Carbopol 974 as a gelling agent, Tween 20 as an emulsifier, and propylene glycol as a penetration enhancer, with methyl paraben and propyl paraben serving as preservatives. Capsaicin, a hydrophobic drug, was effectively incorporated into the formulation. The prepared emulgels were evaluated for their physical appearance, pH, viscosity, spreadability, in-vitro drug release, and drug content. The formulations demonstrated good stability, homogeneity, and were free from irritation, redness, itching, or allergic reactions. In-vitro drug release studies revealed a maximum drug release of 90.51% over 6 hours. Among the developed formulations, batch F1 exhibited the best drug release profile and was selected as the optimized formulation. These findings indicate that the formulated capsaicin emulgel is a promising candidate for topical drug delivery.

Keyword: Emulgel, Capsaicin, Gel, Rheumatoid Arthritis, analgesic.

I. INTRODUCTION:

Topical drug delivery system is a route of administering drugs via the skin to provide topical therapeutic effects. As skin is one of the largest and most superficial organs in the human body, pharmacists utilize it to deliver various drugs. This system usually provides a local effect on certain positions of the body. A topical medication is a medication that is applied to a particular place on the body. These topical preparations are of different classes like gel, cream, lotion, liniment, solution, Ointments etc. In specifically the topical dosage formulation are tend to be easier in application, convenient for usage, should be conventional on its usage. An increased dose of medication is applied where it is needed. There are reduced side effects and toxicity to other organs compared to systemic medications. The mechanism of action of form of preparation usually requires the use of suitable tools such as a skin brush or a spray tube that creates a mucous membrane and then evaporates quickly, leaving a layer of medicine on the skin to be treated.

Emulgels, a combination of emulsions and gels, provide an effective drug delivery system that enhances the solubility and bioavailability of both hydrophilic and lipophilic drugs. This dosage form overcomes the limitations of conventional gels in delivering hydrophobic drugs by incorporating a gelling agent into the water phase, transforming a traditional emulsion into an emulgel. Both oil-in-water (o/w) and water-in-oil (w/o) emulsions serve as carriers for topical drug delivery, offering controlled and sustained release of active pharmaceutical ingredients. The internal phase of the emulsion acts as a drug reservoir, gradually releasing the drug through the external phase to the skin. Additionally, the gel matrix forms a cross-linked network that encapsulates drug particles, ensuring a prolonged and controlled release. Emulgels exhibit bioadhesive properties, extending the contact time of the medication with the skin, thereby enhancing therapeutic efficacy. Depending on the type of emulsion used, emulgels can be classified as macroemulgels, microemulgels, or nanoemulgels. This versatile formulation is widely utilized for delivering various therapeutic agents, including NSAIDs, antifungal, antibacterial, and antiviral drugs, making it a promising candidate for topical drug administration.

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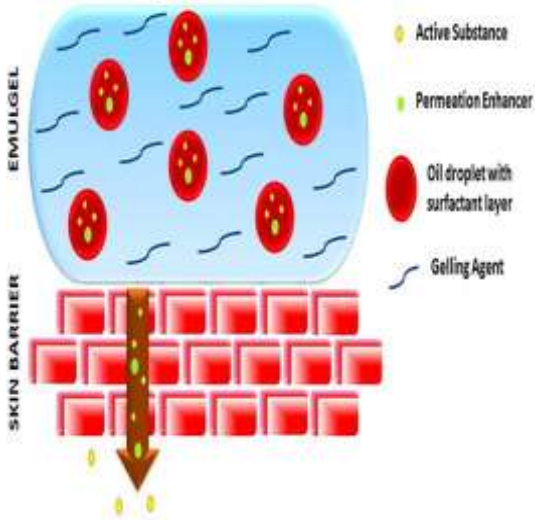

Fig 1: Emulgel Penetration Through Skin

II. DISEASE PROFILE:

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disorder that primarily targets the joints, distinguishing it from osteoarthritis, which results from mechanical wear and tear. RA arises when the immune system erroneously attacks the synovium, the membrane lining the joints, leading to persistent inflammation, tissue damage, pain, swelling, stiffness, and potential joint deformity. The condition often initially manifests in the hands and feet, typically affecting the same joints on both sides of the body. Common symptoms include joint stiffness, particularly upon waking or after prolonged inactivity, along with fatigue and a general sense of malaise. According to the Rheumatoid Arthritis Support Network, RA affects approximately 1% of the global population, with over 1.3 million cases in the United States alone. The incidence of RA has been increasing worldwide and is projected to continue rising. Understanding RA's pathophysiology and prevalence is crucial for developing effective treatment strategies and improving patient outcomes.

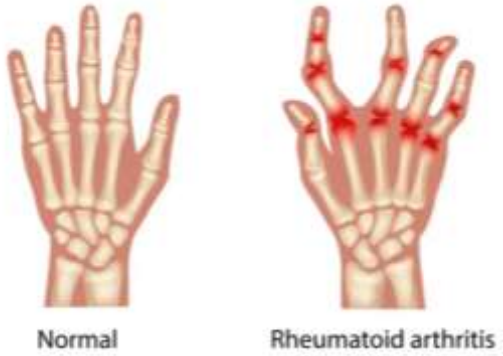

Fig 2: NORMAL/HEALTHY BONE (VS) ABNORMAL HAND BONE

III. PLANT PROFILE:

Synonym: Hari mirch, Habanero peppers, jalapenos, serrano peppers, thai chillies, bell pepper, cayenne pepper

Biological source: Green chilli extract is obtained by the solvent extraction of Capsicumannum. L **Family**: Solanaceae

Geographical source : green chilli is also known as chilli peppers or capsicums, are believed to have originated in Central or South America and where first cultivated in Mexico.

1.1 TAXONOMICAL CLASSIFICATION:

- Kingdom- Plantae
- Phylum- Spermatophyte
- Class- Dicotyledonae
- Order- Solanales
- Family- Solanaceae
- Genus- Capsicum
- Species- Capsicum annuum

3.2 CHEMICAL CONSTITUENT:

- Capasaicinoid
- Carotenoid
- Flavanoids
- Vitamins
- Alkaloids
- Phenolic compounds
- Steroid saponins
- Essential oils

Fig 3: GREEN CHILL

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IV. MATERIALS AND METHODS:

4.1 PLANT COLLECTION:

Capsicum annum plant fruits was obtained from vilanallur village, Thiruvannamalai district, Tamil Nadu India. It was identified and authenticated CAPTAIN SRINIVASA MURTHI CENTRAL AYURVEDA RESEARCH INSTITUTE (Centrecouncil for research in ayurvedic science, ministry of AYUSH, government of India). A government hospital campus, Arumbakkam chennai-600106.The fruit was washed thoroughly with tap water, shade dried and grained using mortar and pestle. The powder was then stored in an air tight container until further uses.

4.2 MACERATION METHOD:

The Maceration process is an ancient technique in which the whole or selected parts of a vegetable sample(or other natural extracts) are kept in contact with a specific solvent, for certain period of time, which can range from some hours to days, at room temperatures. Maceration is a convenient, simple inexpensive, and favourable technique, especially in the case of small-scale extraction, such as that at laboratory scale. It is based on the induction of the mass transfer with shaking until the solid/liquid equilibrium is reached. this technique usually requires second step for the concentration of the extract. Maceration is also a well-known technique used for the preparation of the tonics. It is carried out in closed vessels with the occasional mixing and involves several consecutive steps: grinding of the plant material, immersion of grinded material into solvent, removing the solvent, and pressing of the sample in order to recover crude extract. Those steps are performed for:

Increasing diffusion of desired compounds from plant material to solvent. Removing concentrated solution from the surface of plant material which actually increases extraction yield. Despite its simplicity, maceration possess many disadvantages. They acquire solvents for the extraction which are usually long with the possibility of degradation of the compounds of interest due to their thermolability and/or due to the oxidation. The technique is insufficiently selective and requires additional steps for separation and requires additional steps for separation and/or purification of the compounds of interest, Final extracts usually contain solvents' residues whose presence is not desirable due to health and products safety issues.

Fig 4: MACERATION EXTRACT

4.3 FORMULATION OF CAPSAICIN EMULGEL:

Ingredients	F1	F2	F3
Capsaicin	**0.1%**	0.1%	0.1%
Carbopol 974	**1%**	-	-
Carbopol 930	**-**	2%	-
Xanthum gum	**-**	-	1%
Span 80	**1%**	1%	1%
Liquid paraffin	**7.5%**	7.5%	7.5%
Tween 80	**1%**	1%	1%
Propylene glycol	**5%**	5%	5%
Methyl paraben	**0.03%**	0.03%	0.03%
Ethanol	**2.5%**	2.5%	2.5%
Water	**Q.S**	Q.S	Q.S

Table 1: FORMULATION TABLE FOR EMULGEL

Procedure: The preparation of emulgel involves a systematic process integrating both emulsion and gel formation to enhance drug delivery efficiency. The method consists of four primary steps:

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preparation of the oil phase, preparation of the aqueous phase, formulation of the emulsion, and incorporation of the gelling agent. The oil phase is prepared by mixing the oil component (e.g., liquid paraffin) with an emulsifier (e.g., Span 80, Tween 20) and heating it to 60-70°C for effective emulsification. Simultaneously, the aqueous phase is prepared by dissolving a humectant (e.g., glycerine) and preservative (e.g., methyl paraben) in purified water, followed by the dispersion of the gelling agent (Carbopol 940) while maintaining a similar temperature range to ensure proper hydration. The oil phase is then gradually introduced into the aqueous phase with continuous stirring to form a stable emulsion. Finally, after slight cooling, the gelling agent is incorporated, and the pH is adjusted using Triethanolamine (TEA) drop wise, allowing the emulsion to thicken into a gel-like consistency. This structured approach ensures the formation of a homogeneous, stable emulgel suitable for topical drug delivery.

Fig 5: EMULGEL

4.4 EVALUATION PARAMETERS:

The prepared emulgel is evaluated for Organoleptic characteristics, pH, Spreadability Co-efficient, Melting point, Viscosity, Stability Studies, UV Calibration curve, IR spectroscopy, Skin Irritation Test, In-vitro Drug Release.

Organoleptic characteristics: The prepared emulgel formulation was inspected visually for their color, appearance and consistency.

pH: The pH of the emulgel was determined by utilization a digital pH meter (HI-9812.5 pH / EC / TDS / ℃ portable meter, Romania). 1g of emulgel was dissolved in distilled water, and the volume mase up to 100ml (ie. 1% of prepared emulgel formulation), and then pH determination has to be prepare. The pH is then calculated using the expression

pH = -log [H_3O^+]

Spreadability Co-efficient: Spreadability is checked by "slip" and "drag" character of emulgel. To determine spreadability, the apparatus consisting a wooden block is provided by a pulley at one end. In the block a round glass is fixed, 2g of emulgel is displaced on it, and it is covered with an another glass slide as a sandwich. 1kg of weight is placed on it and the spreadability has to be check. It is calculated by using the following formula:

S=M×L/T

Where,

M- it is the weight in the pan,

L-is the length moved by glass slide,

T- time taken to separate the slide.

Melting point: Melting point determination is a laboratory procedure that measures the temperature at which substance melts. It is used to identify a substance or determine its purity.

Viscosity: Measurement of viscosity was done by cone and plate viscometer VR 3000 (Viscotech Spain) by choosing the appropriate spindle number L4 and rpm (100 rpm) at room temperature. An appropriate amount of each emulgel formulation was kept in a suitable beaker and the spindle groove was dipped, and the rpm was set. Viscosity measurement was started and the reading was measured after 1 minute.

Stability Studies: The prepared emulgels was packed in aluminum collapsible tubes (5g) stored in extreme conditions and subjected to stability studies at 5℃, 25℃/ 60% RH 30℃/ 65% RH and 40℃/ 75% RH for a period of 3 months. Samples was withdrawn at 15day time intervals and evaluated.

UV Calibration curve: A calibration curve for emulgel is critical component of analytical method validation. Here's a detailed overview:

Calibration curve parameters:

1. Analyte: Active Pharmaceutical In gradient (API)
2. Concentration range:Typically50 - 150 % of the target concentration
3. Standard solution: Prepare 5 to 7 standards with known concentrations

IR spectroscopy: IR spectroscopy is a chemical analysis technique that measures how infrared radiation interacts with matter. Its used to identify and study chemical substances and functional groups in solids, liquids, and gases. This IR

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spectroscopy can identify unknown substances by comparing their IR spectrum to spectral libraries. The capsaicin emulgel sample is undergone IR spectroscopy for identifying the molecules present in it.

Skin Irritation Test: A skin irritation test is a method used to assess how likely a substances is to causes irritation or damage to the skin by applying a small amount to a test area and observing any reactions like redness, swelling, or itching over a set period oftime, typically done using a patch test on human volunteers or in vitro models with reconstructed human skin.

In-vitro Drug Release: The invitro drug release studies was carried out using a modified Franze Diffusion (FD) cell. The formulation was applied on dialysis membrane which was placed between donor and receptor compartment of the FD cell. Phosphate buffer pH 7.4 was used as a dilution media. The temperature of the cell maintained at 37 ℃ by circulating water jacket this whole assembly was kept on a magnetic stirrer and the solution was stirred continuously using a magnetic bead. The similar blank set was run simultaneously as a control. Sample (5ml) was withdrawn at suitable time intervals and replaced with equal amounts of fresh dissolution media. Samples was spectrophotometrically at 285nm and the cumulative % drug release was calculated.

V. RESULTS AND DISCUSSION:

5.1 ORGANOLEPTIC CHARACTERISTICS:

S. NO	BATCH CODE	COLOR	PHASE SEPARATION	HOMOGENICITY	ODOUR	CONSISTENCY
1.	F1	Pale green	No	Homogenous	Pungent smell	Creamy
2.	F2	Pale green	No	Homogenous	Pungent smell	Creamy
3.	F3	Pale green	No	Homogenous	Pungent smell	Creamy

Table 2: ORGANOLEPTIC CHARACTERISTICS

F1 **F2** **F3**

Fig 6: EMULGEL

5.2 MELTING POINT, pH & VISCOSITY:

S.NO	OBSERVATION	REPORTED STANDARD	pH VALUE (± S.D)	VISCOSITY(CPS) (±S.D)
1.	149. 5℃	144℃ to 152℃	6.2 ±0.10	2161±9.01
2.	148.7℃	144℃ to 152℃	5.9±0.15	2168±4.58
3.	146.3℃	144℃ to 152℃	6.3±0.35	2190±6.50

Table 3: MELTING POINT, pH & VISCOSITY

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5.3 SPREADABILITY:

S.NO	FORMULATION	TIME (Sec)	LENGTH (cm)	WEIGHT (gm)	SPREADABILITY S=M.L/T (gm.cm.Sec)
1	F1	25	7	50	14
2	F2	23	7	50	15.21
3	F3	26	7	50	13.46

Table 4: SPREADABILITY

5.4 GLOBULE SIZE DETERMINATION:

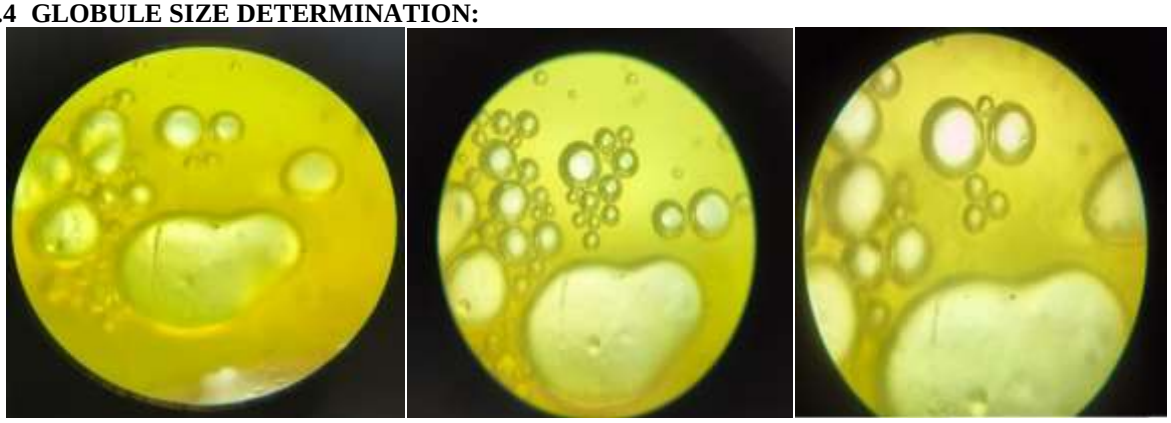

Fig 7: GLOBULE SIZE 5x, 10x & 15x MAGNIFICATION

5.5 DRUG EXCIPIENTS COMPATABILITY STUDIES:

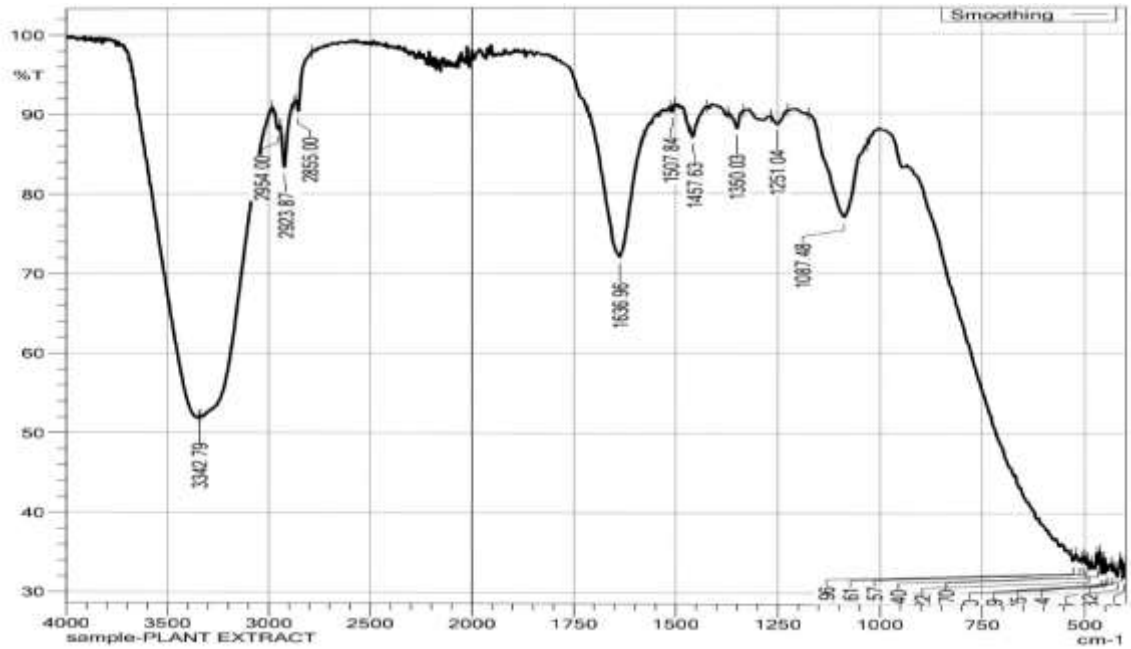

Fig 8: IR SPECTREUM OF EMULGEL

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5.6 UV SPECTRUM:

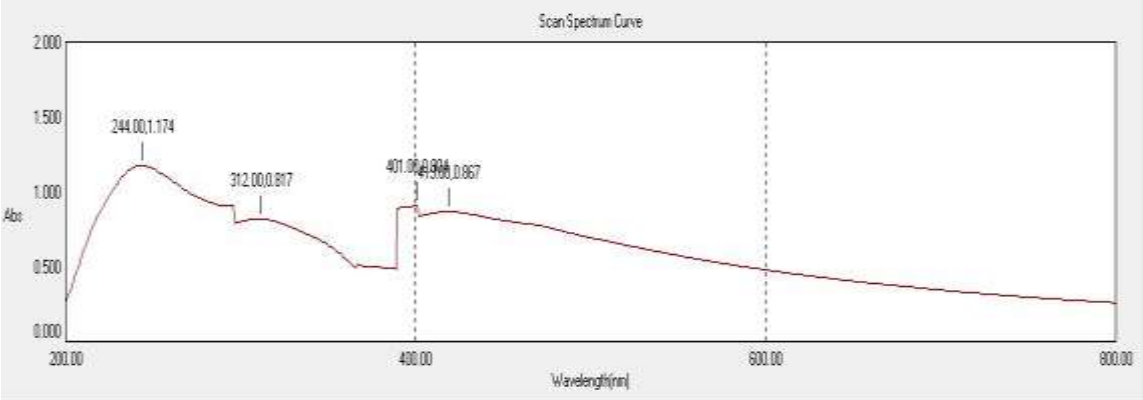


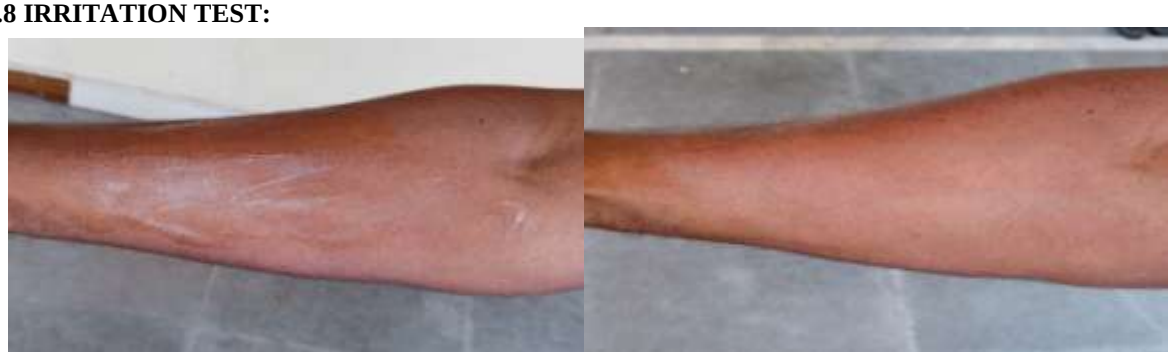
Fig 9: UV SPECTRUM

5.7 SOLUBILITY:

Solvents	Solubility
Distilled water	Partially insoluble (less than 1 part)
Dichloromethane	Freely soluble (1-10)
Choloroform	Soluble (10-30)
Methanol	Soluble (10-30)
Ethanol	Sparingly soluble (30-1000)

Table 5: SOLUBILITY

5.8 IRRITATION TEST:



Capsaicin emulgel was applied Irritancy test is passed, there is no Irritation

Fig 10: SKIN IRRITATION TEST

5.9 IN-VITRO DRUG RELEASE STUDIES:

S.no	Time (hrs)	F1 % drug released	F2 % drug released	F3% drug released
1	1	0.9	0.7	0.5
2	2	9.84	9.76	9.67
3	3	24.57	23.86	23
4	4	43.43	42.32	40.99
5	5	66.06	64.74	63.16
6	6	90.51	89.08	87.24

Table 6: IN-VITRO DRUG RELEASE

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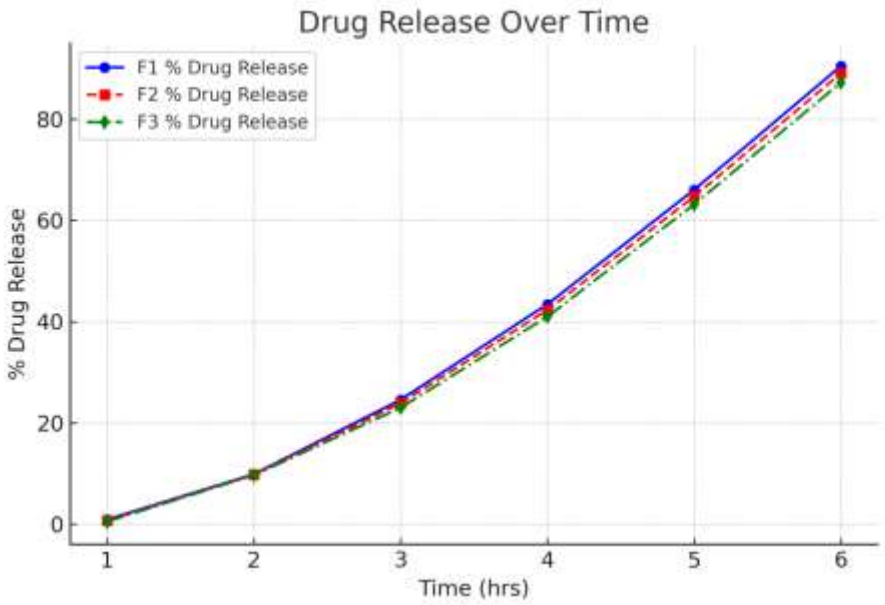

Fig 11: IN-VITRO DRUG RELEASE (GRAPH 1)

VI. CONCLUSION:

In the present study, attempt is been made to formulate the topical drug delivery system of capsaicin emulgel. Emulgel was developed using gelling agent carbopol 974 and tween 20 used as emulsifier, propylene glycol used as penetration enhancer, methyl paraben and propyl paraben used as preservative and capsaicin has a hydrophobic drug. All the formulations have passed all the evaluation with good values. The formulation was found to be stable and homogenous in nature, pH and there was no irritation, no redness, no itching and no allergy. The prepared emulgel was evaluated for their physical appearance, pH determination, viscosity, spreadability, in-vitro drug release and drug content. Physical characteristics of all the prepared emulgel was acceptable. To investigate the rate and duration of drug release from emulgel, in-vitro drug release and of the test formulation was done. In-vitro testing reveals a maximum release of 90.51% in 6 hours. In vitro release of the tests formulation was performed to determine drug release rate from emulgel. Among the various formulation developed F1 formulation was found to better and its thus optimized. When compared to all other formulation, the formulation batch F1 shows better drug release.

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