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Formulation and Evaluation of Organo-Transdermal Gel of Drug Ibuprofen

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ABSTRACT:

The current research project is centered on the development and assessment of an Ibuprofen topical gel made with Guar gum as the polymer and Carbopol 940 as a penetration enhancer. [Gels were made by dispersing the polymers in a solution of guar gum and isopropyl myristate, along with Carbopol 940, glycerol as aqueous agents, and potassium sorbate as preservative, and different concentrations of ibuprofen, all while maintaining magnetic stirring. Triethanolamine was then added to the dispersion to neutralize it and make it viscous. Ibuprofen - Guar gum gels were discovered to be homogeneous and to have adequate drug loading. All of the gel compositions' pH values fell within the range of neutral pH, which is suitable for skin. And it was discovered that the compositions' viscosity was suitable for topical use the drug content of the nine formulations was found in the range of 80% to 90% which shows efficient drug loading. The compatibility study showed that the major peaks in FTIR spectra of the pure drug were found to be intact in their physical mixture. Hence there is no interaction between the drug and Carbopol, drug and Guar Gum in their physical mixture. Guar gum can be effectively used as a polymer with Carbopol 940.

Keywords: Ibuprofen, Guar gum, Carbopol 940, Transdermal gel.

INTRODUCTION

The topic of transdermal drug administration is particularly relevant, especially in light of the recent advancement of novel medications for the management of various inflammatory skin conditions. In an order to reduce both global and local side effects, the goal of optimal pharmacological therapy is to achieve effective drug concentration at the target for a predetermined amount of time. The features of the skin's drug disposition make it the most intriguing organ. [7] Due to its ease and safety for Skin chemotherapy, topical administration of medicines is typically the method of choice. Numerous research papers from the last few decades have shown the promise of regulated and ongoing drug delivery systems. Additionally, a number of methods have been tried to lengthen the therapeutic effect of transdermal medicines and boost their absorption. [8]

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The Skin is a unique organ, both anatomically and physiologically, containing several widely varied structures with different physiological functions that render the organ highly impervious to foreign substances. Conventional drug delivery such as creams, Lotions ointment, show some drawbacks such as, sometimes ointment is not preferred due to cosmetics concerns, creams contain more preservatives which provide irritation and stinging and lotions are not able to make a protective layer over the skin. The absorption of drugs in the skin can be through some mechanisms that ensure the proper functioning of the skin and by other concomitant factors like dry skin, oily skin, the evaporation rate of the solvent when applied to the skin, non-productive absorption/adsorption, limitation of different receptors helping in penetration and different materials permeability used in the gel.[9]

MATERIALS AND METHOD

I. MATERIALS

Ibuprofen Guar Gum, Carbopol 940, Isopropyl Myristate, and Glycerol were obtained from laboratory chemicals.

II. EXPERIMENTAL

- **Identification of Drug**
  - **By UV Spectroscopy:**

10 mg drug dissolve in 100 ml of 0.1N NaOH it's an obtained stock solution of 100 micrograms/ml. Then from the stock solution, 10 ml of solution is taken and the volume is made up to 100 ml with 0.1 N NaOH solution and scanned under UV between 200 to 400 nm wavelength**.** [10,12]

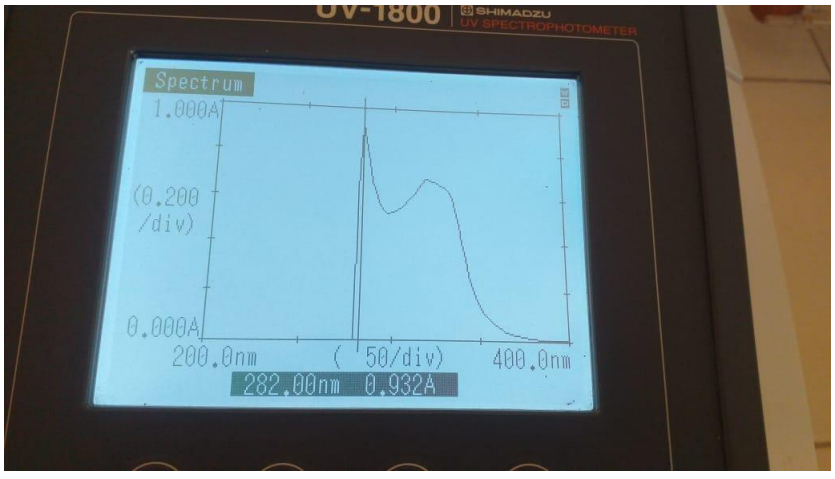

Figure No. 1: Ibuprofen Spectrum by UV Spectroscopy

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- **By melting point determination**

Melting Point determination is one of the formulation properties in which the temperature at which it changes state from solid to liquid at atmospheric pressure. During the melting process, the solid and liquid can exist in equilibrium. The Melting point of the Ibuprofen drug is determined by using Melting Point Apparatus. [11]

Table No. 1: Melting Point of Ibuprofen

Drug	Observed
Ibuprofen	76.4℃

- **Preparation of Calibration Curve:**

- **Preparation of calibration curve of drug with Distill Water**

A Stock Solution of 1 mg/ml of Ibuprofen was prepared by dissolving 100 mg of the drug in 100 ml of Distill Water and working standards namely 2, 4, 6, 8, 10 and12 mcg/ml of the final solution were prepared by using appropriate dilutions. Absorbances of the solutions were measured at 282 nm and the calibration curve was developed by plotting concentration on X-axis and absorbance on Y-axis. The absorbance of different diluted solutions was measured in UV-Visible Spectrophotometer at 282 nm.[12]

Calibration curve of Ibuprofen with Distill Water

Table No. 2: Absorbance data of Ibuprofen with calibration curve at 280nm.

S. No.	Concentration (µg/ml)	Absorbance
1.	2 µg/ml	0.387
2.	4 µg/ml	0.579
3.	6 µg/ml	0.788
4.	8 µg/ml	0.944
5.	10 µg/ml	1.146
6.	12 µg/ml	1.333

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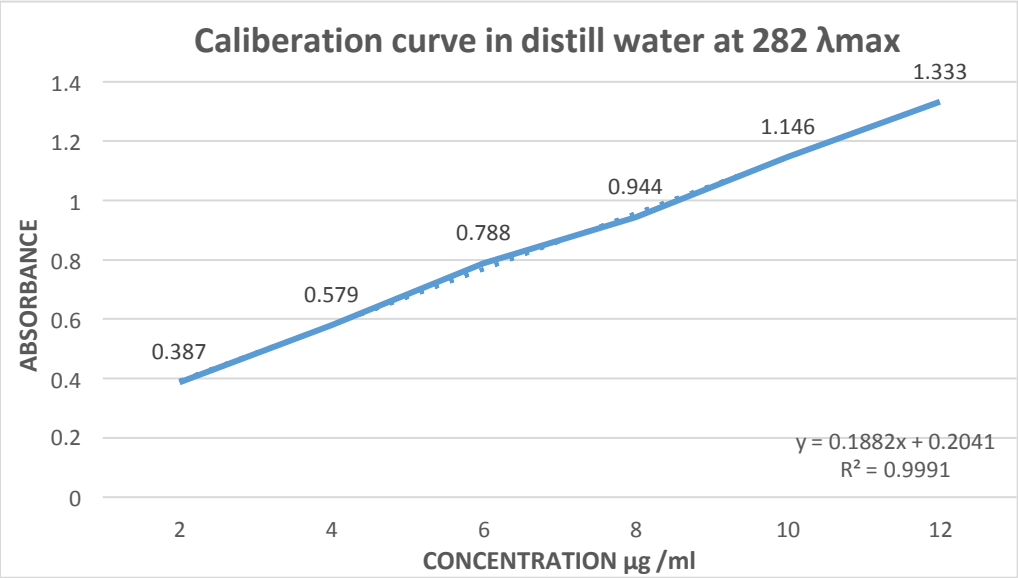

Fig No. 2 Calibration graph of Ibuprofen in Distill water

- **Preparation of calibration curve of drug with phosphate buffer(pH7.4)**

A Stock Solution of 1 mg/ml of Ibuprofen was prepared by dissolving 100 mg of the drug in 100 ml of pH 7.4 Phosphate buffer Solution and working standard namely 2, 4, 6, 8, 10 and12 mcg/ml of the final solution were prepared by using appropriate dilutions. Absorbances of the solutions were measured at 282 nm and the calibration curve was developed by plotting concentration on X-axis and absorbance on Y-axis. The absorbance of different diluted solutions was measured in UV-Visible Spectrophotometer at 282 nm.[12]

Calibration curve of Ibuprofen with PBS (7.4)

Table No. 3: Absorbance data of Ibuprofen with calibration curve at 282nm

S. No.	Concentration(µg/ml)	Absorbance
1.	2 µg/ml	0.458
2.	4 µg/ml	0.688
3.	6 µg/ml	0.999
4.	8 µg/ml	1.255
5.	10 µg/ml	1.597
6.	12 µg/ml	1.788

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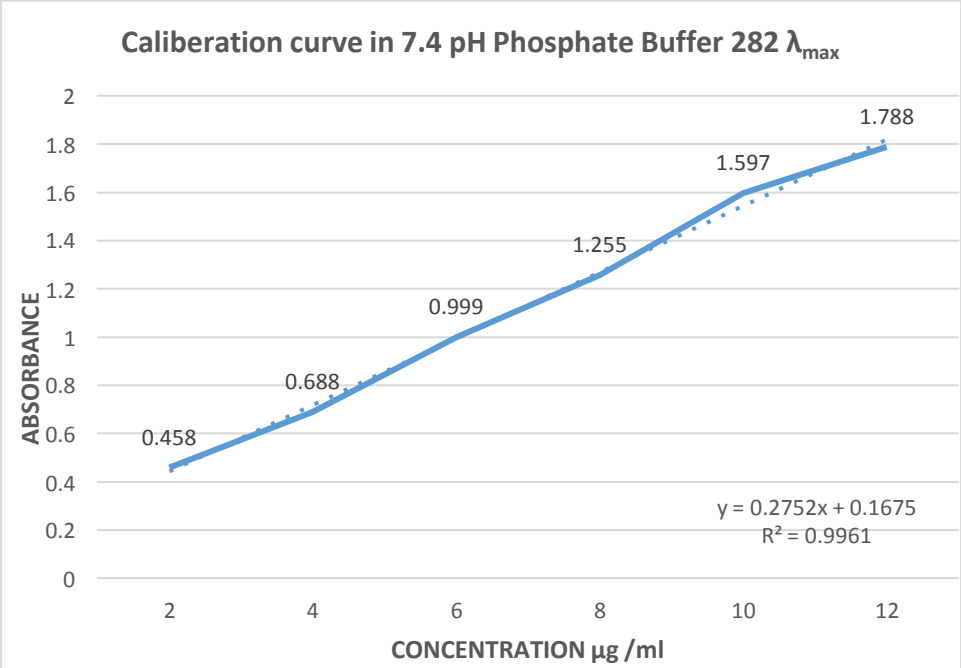

Fig No. 3 Calibration graph of Ibuprofen in phosphate buffer pH 7.4

- **Preparation of calibration curve of drug with 0.1 N NaOH Solution**

A Stock Solution of 1 mg/ml of Ibuprofen was prepared by dissolving 100 mg of the drug in 100 ml of 0.1 N NaOH solution and working standards namely 2, 4, 6, 8, 10 and12 mcg/ml of the final solution were prepared by using appropriate dilutions. Absorbances of the solutions were measured at 282 nm and the calibration curve was developed by plotting concentration on X-axis and absorbance on Y-axis. The absorbance of different diluted solutions was measured in UV-Visible Spectrophotometer at 282 nm.[12]

Calibration curve of Ibuprofen with 0.1N NaOH

Table No. 4: Absorbance data of Ibuprofen with calibration curve at 282nm

S. No.	Concentration(µg/ml)	Absorbance
1.	2 µg/ml	0.388
2.	4 µg/ml	0.599
3.	6 µg/ml	0.894
4.	8 µg/ml	1.119

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5.	10 µg/ml	1.347
6.	12 µg/ml	1.577

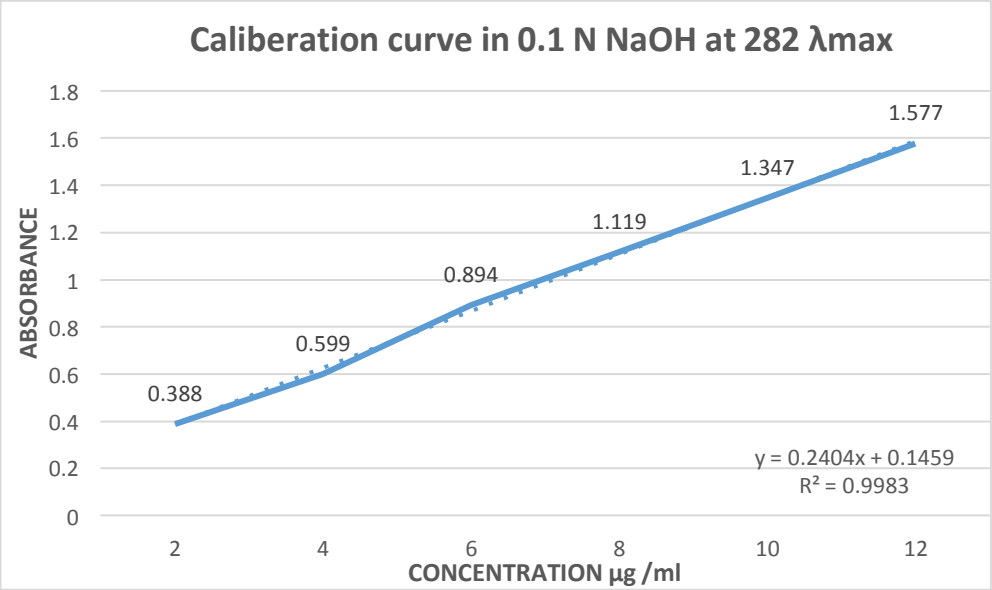

Fig No. 4 Calibration graph of Ibuprofen in 0.1 N NaOH Solution

- **Solubility studies of the drug:**

The Term Solubility is defined as the maximum amount of solute that can be dissolved in a given amount of solvent to form a homogenous system at the specified temperature and Specific Pressure from a Saturated Solution**.** [13]

Procedure:

To Prepare different solutions Water, pH 7.4 Phosphate Buffer, NaOH, Ethanol, and Chloroform. The drug material is added to the above solutions till Supersaturated Solution from the Mixture is shaken for 10 min till 2 hours and after 24 to 72 hrs. Filter the mixture Take Filtrate and Give Absorbance to detect the Concentration of the Drug is Soluble in Different Solutions.[13]

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RESULT:

Table No. 5: Solubility data of Ibuprofen

Solubility studies of Ibuprofen with different solvents

- Ibuprofen

S. No.	Solvents	Solubility (mg/ml)	Inference
1	Distilled Water	0.8 mg/ml	Insoluble
2	PBS (PH 7.4)	5.1 mg/ml	Slightly Soluble
3	NaOH	10.3 mg/ ml	Freely Soluble
4	Ethanol	11.4 mg/ml	Freely Soluble
5	Chloroform	8.5 mg/ml	Slightly Soluble

- **Drug and Excipient Interaction Studies:**

The raw material pure drug, a physical mixture of excipient, as well as polymer and formulation powder samples, were characterized by FTIR spectroscopy in the range of 4000 – 400 cm-1 using the KBr pellet method. [14,20]

Result:

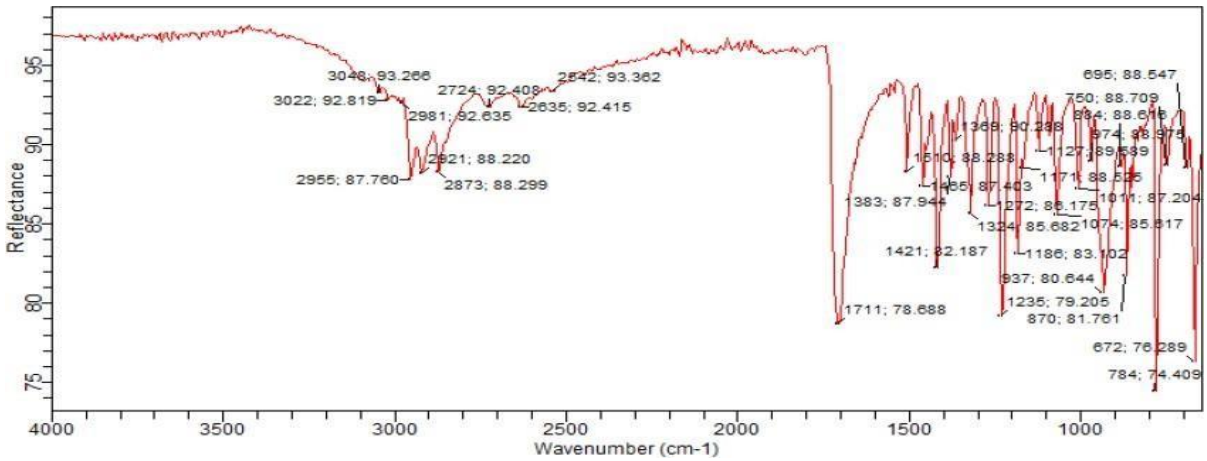

Figure No. 5 FTIR Graph of Drug Ibuprofen

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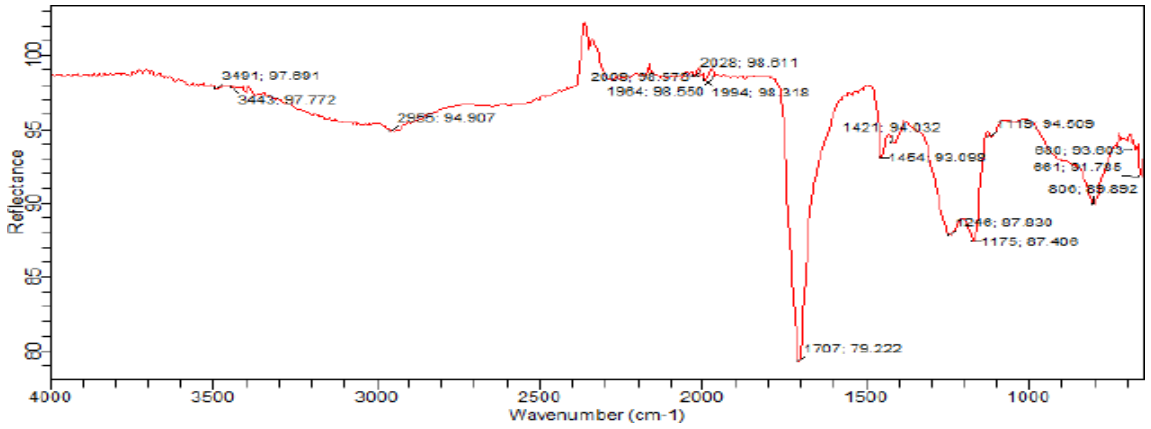

Figure No. 6 FTIR Graph of Drug Ibuprofen with Carbopol

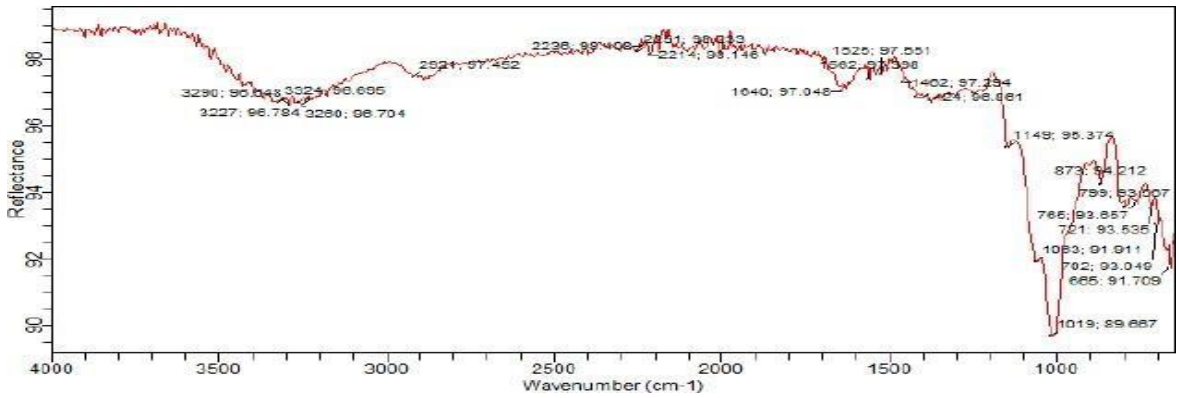

Figure No. 7 FTIR Graph of Drug Ibuprofen with Guar Gum

The different formulations of Excipients, drug, and their physical mixtures were found to be stable under refrigerated conditions, and room temperature. As there were no changes in physical characteristics. Hence it was inferred that the selected excipients are compatible with the drug.

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III. Formulation:

- **Selection of Excipient for Organo-Transdermal Gel**

Table No. 6: List of excipients used in the Formulation of Organo-Transdermal Gel

S.NO.	NAME OF EXCIPIENT	USE
1	Ibuprofen	NSAIDs (Non-steroidal anti-inflammatory drugs)
2	Guar Gum	Gelling Agent, Polymer
3	Carbopol 940	Emulsifying agent
4	Potassium Sorbate	Preservative
5	Triethanolamine	pH Adjuster
6	Glycerol, PEG, Isopropyl Myristate, and Distill Water	Solvents

- **Formulation of Organo-Transdermal Gel:**

Table No. 7: Composition of Organo-Transdermal Gel

Content & Batch	Ibuprofen	PEG	Guar Gum	Isopropyl Myristate	Carbopol	Glycerol	Potassium Sorbate	D.W	Triethanol amine
F1	1	10	5	50	5	20	0.5	50	Q. S.
F2	1	10	5	50	10	20	0.5	50	Q. S.
F3	1	10	5	50	15	20	0.5	50	Q. S.
F4	1	10	10	50	5	20	0.5	50	Q. S.
F5	1	10	10	50	10	20	0.5	50	Q. S.
F6	1	10	10	50	15	20	0.5	50	Q. S.

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F7	1	10	15	50	5	20	0.5	50	Q. S.
F8	1	10	15	50	10	20	0.5	50	Q. S.
F9	1	10	15	50	15	20	0.5	50	Q. S.

- **Procedure of Organo-Transdermal Gel**

1. Guar Gum and Isopropyl Myristate were mixed in the desired quantity with the help of a magnetic stirrer. The mixture was allowed to stay overnight.
2. On another hand Ibuprofen, Glycerol, Carbopol, and Potassium Sorbate were dissolved in cold distilled water and mixed with Magnetic Stirrer.
3. Next Day both the above solution was mixed with PEG and Distilled water.
4. pH of the gel was adjusted with Triethanolamine.

IV. Evaluation of Formulation:

- **Physico-chemical characterization**
- **Visual inspection and clarity:**

Visual appearance and clarity were tested under a fluorescent light against a white and black background for the presence of any particulate matter**.**

- **pH determination:**

pH of the organo-transdermal gels after the addition of all ingredients was measured using a digital pH meter.

RESULT:

Table No. 8: Physico-chemical characterization

S.no.	Formulation	Clarity	Color	pH
1	F1	CLEAR	YELLOWISH	7.28
2	F2	CLEAR	YELLOWISH	7.42
3	F3	CLEAR	YELLOWISH	7.43
4	F4	CLEAR	YELLOWISH	7.09
5	F5	CLEAR	YELLOWISH	7.13
6	F6	CLEAR	YELLOWISH	7.44
7	F7	CLEAR	YELLOWISH	7.20
8	F8	CLEAR	YELLOWISH	7.10
9	F9	CLEAR	YELLOWISH	6.85

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- **Drug Content:**

1 gm of gels was prepared and weighed accurately dissolved in 10 ml of 0.1 N NaOH and filtered. Then 1 ml of filtrate was taken diluted up to 100 ml by 0.1 N NaOH and was observed in an Ultraviolet UV spectrophotometer at 282 nm. [15,16,17]

RESULT:

Table No. 9: Drug – Content

S.no.	Formulation	Concentration of Ibuprofen (%)
1	F1	94.06 +/- 1.36
2	F2	92.66 +/- 0.84
3	F3	94.16 +/- 0.79
4	F4	93.53 +/- 2.10
5	F5	90.13 +/- 1.91
6	F6	95.78 +/- 3.56
7	F7	91.83 +/- 4.35
8	F8	92.66 +/- 2.99
9	F9	93.88 +/- 4.59

The result of drug content is (shown in the table). The organo-transdermal gel formulations with different batches (F1-F9) show good drug content but batch F6 shows the best drug content from the rest formulations

- **Spread-ability:**

It is one of the criteria for the gels that it should have good spread-ability. It is expressed by the extent of the area to which the gels spreads while applied on the skin or affected part. The effectiveness depends upon the value of spread-ability. It is expressed in time (sec) taken by two slides to slip from the gel and placed in between the slides under the direction of a certain load. Lesser the time taken for the separation of two slides better is the spread-ability. It is calculated by using the formula: $S = M*L /T$

Where M is the weight tide to the upper slide, L is the length of the glass slide and T is the time is taken to separate the slides. [18]

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RESULT:

Table No. 10: Spread-ability

S. No.	Batch	Spread-ability (g/cm.sec)
1	F1	4.08 +/- 1.66
2	F2	4.88 +/- 0.69
3	F3	5.54 +/- 2.39
4	F4	3.59 +/- 0.94
5	F5	3.77 +/- 1.01
6	F6	5.64 +/- 2.83
7	F7	2.89 +/- 1.22
8	F8	3.08 +/- 2.77
9	F9	4.77 +/- 0.35

- **Rheological Study:**

Viscosity serves as the benchmark for rheological research. The gel's viscosity is measured using a Brookfield viscometer. Gels were transferred into the jar, and spindle number 63 revolved at 20 rpm while being lowered so as not to touch the end of the jar. The results were recorded. The reverse value was also noted, and an average of these two readings was calculated. By multiplying the reading with the variables listed in the Brookfield Viscometer catalogs, the viscosity of gels was determined. Spindle size 64 is employed.[19]

Table No. 11: Viscosity:

S. No.	Batch	Viscosity
1	F1	11750cP
2	F2	12300cP
3	F3	10500cP
4	F4	14950cP
5	F5	12850cP

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6	F6	15400cP
7	F7	14600cP
8	F8	13000cP
9	F9	13150cP

V. Conclusion:

Ibuprofen is an NSAID (non-steroidal anti-inflammatory drug), used for the treatment of rheumatic pain caused by problems with muscles, tendons, joints, or bones. It is also used for period pain, toothache and migraines as well. It was formulated as an organo-transdermal gel using polymers such as Guar gum as polymer, and Carbopol 940 as a gelling agent in a combination of suitable preservatives & solvents. The characterization of the drug sample was done using spectrophotometric analysis and melting point determination. All the observations and recorded data were identical to the values reported in the literature. Calibration curves of Ibuprofen in 0.1 N NaOH, distilled water, and phosphate buffer (pH 7.4) were prepared using a double-beam UV-visible spectrophotometer (Shimadzu 1800). It is easy for the administration to afford and decreased frequency of administration resulting he better patient compliance and acceptance. Therefore, thought worthwhile to develop an organo-transdermal gel formulation using a suitable polymer to effectively deliver the drug into the systemic circulation with sustained and prolonged release and enhanced drug bioavailability. It is observed from formulation F6 which shows a drug content of 95.78 % and has good viscosity and spreading capacity. Thus, it can be concluded that the drug given in the form of an organo-transdermal gel of Ibuprofen provides better patient compliance and an effective mode of treatment.

VI. Acknowledgement:

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References

[1]. Vyas PS, Khar KR, "Drug Delivery System", 2012;2: 397-399.
[2]. Robinso JR, Lee HL, "Controlled drug delivery fundamentals and applications", 1987; 2: 524-552.
[3]. Aqui SY, Ali A, "Matrix type transdermal drug delivery systems of metoprolol tartrate: In vitrocharacterization" Acta Pharm, 2003; 119-125.
[4]. Baselt R, "Disposition of toxic drugs and chemicals in Man,Foster city" Biomedical Publications, 2008; 8: 758–761.
[5]. Misra AN, "Controlled and novel drug delivery" CBS Publishers and Distributors, 1997; 107-109
[6]. Singh J, Tripathi KP and Sakia TR, "Effect of penetration enhancers on the *in vitro* transport of ephedrine through rat skin and human epidermis from matrix based transdermal formulations" Drug Dev Ind Pharm, 1993;1623-1628.
[7]. Acharya A, Dhakal P, and Khadka D, "Formulation and Evaluation of Transdermal Gel of Lornoxicam and its Delivery by Passive and

ISSN: 2519-9889
Impact Factor: 5.721

Inotophoresis Method: A Comparative Study" International Journal of Pharmaceutical Sciences and Research, 2017

[8]. Takmaz E A, Inal O, Baykara T. Studies on transdermal delivery enhancement of zidovudine.AAPS PharmSciTech. (2009) 10: 88–97.

[9]. Barry B W. Novel mechanisms and devices to enable successful transdermal drug delivery. Eur. J. Pharm. Sci. (2001) 14: 101-114.

[10]. Gondalia R, Mashru R, Savaliya P. Development and validation of spectrophotometric methods for simultaneous estimation of ibuprofen and paracetamol in soft gelatin capsule by simultaneous equation method. International Journal of ChemTech Research 2010; 2(4):1881-85.

[11]. Kumar S, Chawla G, Bansal AK. Spherical crystallization of mebendazole to improve processability. *Pharm Dev Technol.* 2008; 13:559–568.

[12]. Farra H, Letzig L, Gil M, "Validation of a liquid chromatographic method for the determination of ibuprofen in human plasma" Journal of Chromatography, 2002; 780:341–348

[13]. Mohanambal E, Arun K, Abdul HasanSathali A. Formulation and evaluation of pH triggeredin situ gelling system of levofloxacin. Indian J. Pharm. Educ. Res. 2011;45(1): 58-64.

[14]. H. Kono, F. Otaka, M. Ozaki. Preparation and characterization of guar gum hydrogel as carrier material for controlled protein drug delivery. Carbohydrate polymers. (2014) Mar 25; 111:830-840.

[15]. Mohamed A, Amira AM, Mohammed AA and Abdulrhman AO, "An in vivo study of Hypericum perforatum in a niosomal topical drug delivery system" Drug Delivery, 2018; 25:417- 425.

[16]. Jangdey MS, Gupta A and Saraf S: Fabrication, "In-vitro characterization, and enhanced in- vivo evaluation of carbopol- based nanoemulsion gel of apigenin for UV-induced skin carcinoma" Drug Delivery, 2017; 24:1026-1036.

[17]. Ali DF, Ahmed AA, Hamza MY and Mohamed MI, "Microemulsion for Topical Delivery of Fenoprofen Calcium: In-vitro and In-vivo Evaluation Journal of Liposome Research", 2017; 1532-2394.

[18]. MarwaHS, GhadaFM,"Evaluation of Topical Gel Bases Formulated with Various Essential Oils for Antibacterial Activity against MethicillinResistant Staphylococcus Aureus" Tropical Journal of Pharmaceutical Research,2013;12: 877-884.

[19]. Ujwala A, ModaniSH and SinghKH,"Design and Development of Repaglinide Microemulsion Gel for Transdermal Delivery"AAPS PharmSciTech, 2018.

[20]. Nanda S, Saroha K and Sharma B,"Formulation, Evaluation And Optimization Of Transdermal Gel Of Ketorolac Tromethamine Using Face Centred Central Composite Design" International Journal of Pharmacy and Pharmaceutical Sciences,2014;6:0975- 1491.

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