FORMULATION DESIGN AND DEVELOPMENT OF TRANSDERMAL PATCH *OCIMUM SANCTUM* AND ITS PHARMACEUTICAL EVALUATION

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ABSTRACT

Transdermal drug delivery systems have many benefits, due to this, lot of interest has increased in this field nowadays. Main objective of this project is to create a *Ocimum sanctum* (Tulsi) transdermal patch. *Ocimum sanctum* is a very well-known medicinal plant with lot of therapeutic benefits. Investigating *Ocimum sanctum's* potential for controlled transdermal administration of bioactive substances is the goal of this research. The formulation development process involves choosing the best polymers, plasticizers, and permeation enhancers to maximize the physicochemical qualities of the transdermal patch and the drug release characteristics.

This pharmaceutical investigation examined the transdermal patch's effectiveness and value. The examination considered studies on the physiochemical characteristics of the patch, uniformity of the drug content, UV analysis, IR analysis, Thin-Layer Chromatography, and *In-Vitro* Analyis. The data collected provide insight into the efficiency of the patch's delivery of *Ocimum sanctum* extract via the skin.

The results of this study can help in the creation of a unique transdermal patch formulation that makes use of *Ocimum sanctum*. This may help in providing a controlled, prolonged release of bioactive components. If the development & drug testing of such a transdermal patch are successful, *Ocimum sanctum* can be utilised therapeutically to treat several medical ailments.

Keywords: PHYTOCHEMICAL, CHROMATOGRAPHY, SPECTROSCOPY, SPECTRUM, ANTIOXIDANT.

INTRODUCTION:

Due to its many benefits, transdermal medication delivery methods have attracted a lot of attention lately. Improved patient compliance, regulated drug release, and first-pass metabolism prevention are some of these benefits. *Ocimum sanctum* which is popularly known as holy basil or Tulsi, is a very treasured medical herb. This is because of its many curative qualities. The ancient Ayurvedic medical system in India has been using Tulsi from a very long time. Anti-inflammatory, analgesic, antioxidant, and antibacterial activities are some of the the pharmacological effects of *Ocimum Sanctum*.[1]

The formulation design and creation of transdermal patches is a promising method to maximize *Ocimum sanctum's* therapeutic potential. Transdermal patches provide a non-invasive technique to deliver drugs through the skin by avoiding the gastrointestinal route and hepatic metabolism. This method of administration has the benefits of a prolonged medication release, fewer systemic adverse effects, and improved patient comfort. A transdermal patch must carefully consider several factors, including the selection of the right polymers, drug loading techniques, permeability enhancers, and supporting membranes. The formulation must offer a perfect pharmaceutical release profile to ensure the desired therapeutic concentration in the systemic circulation.[2]

The transdermal patch's physical, chemical, and biological properties are all extensively evaluated when it is being tested for medical applications. This includes measuring the patch's homogeneity, thickness, weight change, and medicine content. To evaluate aspects including the patch's durability, skin permeability, and the potential for skin irritation, other *in-vitro* and in vivo studies are also conducted. *Ocimum sanctum* may offer various benefits when used to make transdermal patches. Furthermore, *Ocimum sanctum's* inherent anti-inflammatory and antioxidant properties can help cure several skin diseases and hasten wound healing.[3]

In conclusion, the formulation design and creation of a transdermal patch containing *Ocimum sanctum* is a promising strategy for using the therapeutic potential of this plant medicine. Researchers are working to increase *Ocimum sanctum* chemical transport through the skin using the proper formulation strategies and rigorous pharmacological analyses, which may result in better patient results and novel therapeutic options for a variety of dermatological and systemic disorders.[3]

MATERIALS AND METHODS:

Plant material: *Ocimum Sanctum* extract was collected from Vital Herbs, Uttam Nagar, Delhi. The *Ocimum sanctum* has a purity level of 95%.

Solvent extraction: 50g of dried Tulsi powder were placed in the thimble of the Soxhlet apparatus. 200ml of ethanol was the solvent used. The extraction was continued until the thimble was completely empty of all but the clear solvent. To concentrate the extract, rotavapor was employed. A digital water bath was used to dry the extract until a dark green residue had formed. The following formula was used to determine the % yield of the extract:

Percentage yield = $\frac{Final\ weight\ of\ the\ dried\ extract}{Initial\ weight\ of\ the\ powder} \times 100$

Percentage yield = $\frac{4.5\ g}{50\ g} \times 100 = 9\%$ W/W

The percentage yield was 9% W/W. The extracts were kept in refrigerator till further use.

Phytochemical analysis: Phytochemical analysis is the scientific study of compounds or phytochemicals that are derived from plants or are present in plant materials. It involves the identification, quantification, and analysis of many secondary metabolites, bioactive compounds, and other chemical components found in plants. It is crucial to comprehend the chemical composition and potential health benefits of plants for a few reasons, including medicine, nutrition, and agriculture. Phytochemical analysis of *Ocimum Sanctum* Extract identified numerous specialized components.[4]

Mayer's Test: Add 1% HCL after taking 5 mg of extract. Warm the test tube up gradually.

Ferric chloride Test: Mix 5 mg of the extract with 1 ml of water, 0.5 ml of ammonia solution, and conc. H2SO4.

Lieberman Test: It involves adding 2 ml of chloroform and 2 ml of acetic acid to 5 mg of extract. Add 1 ml of H2SO4 after the test tube has been chilled with ice.

Killer Killani Test: Mix 1 cc of glacial acetic acid with 5 mg of the extract. Add 2% Fecl2 and 1 ml H2SO4 next.

Steroid Test: Mix 5 mg of extract with 1 ml of chloroform and 1 drop of H2SO4 for the test.

Ninhydrin Test: Boil the test tube for two minutes after adding 2 ml of a 0.2% solution of Ninhydrin to the extract.

NaOH Test: Mix 1 ml of 10% NaOH with 5 mg of extract. When the mixture becomes yellow, add 1 ml of HCL.

Benedict's Test: Boil five milligrams of extract with a tablespoon of Benedict's reagent.

Ash Values: A statistic called ash value is used to evaluate herbal remedies and medicinal plants. After a sample has been totally burned or incinerated, it shows the total amount of inorganic residue that is still present. Important information on the quality and purity of herbal materials, as well as the presence of pollutants including heavy metals, minerals, and inorganic salts, is obtained by the assessment of the ash value. Ash value is frequently expressed as a percentage and compares the weight of the original sample to the weight of the ash residue. Ash values can be calculated in one of three ways: Total Ash, Acid-Insoluble Ash, Water-Soluble Ash.[5]

Extractive Values: The extractive value parameter, which is used in the analysis of medicinal plants and herbal products, determines the amount of soluble active components present in each sample. It provides information on the compounds that can be extracted using solvents from

plant material. By utilizing different solvents, the quantity of soluble components found in the sample can be utilized to calculate the extractive value of herbal materials. Information on extraction value using ether, alcohol, and water as solvents is provided below.[6]

TLC Analysis: Thin-Layer Chromatography analysis, or TLC analysis, is a technique widely employed in the study of chemistry to separate and pinpoint the components of a mixture. It is highly useful for figuring out the quantity and purity of various compounds in a sample. In TLC analysis, an adsorbent material (often silica gel or alumina) is thinly deposited on a flat surface, like a glass plate or plastic sheet. The sample mixture is applied in an area or line at the plate's base. The plate is then placed in a developing chamber with a solvent or mobile phase, which via capillary action advances the plate. The mobile phase moves while transporting the various components of the sample mixture. The individual components separate from one another according to their respective affinities for the stationary phase (adsorbent material) and the mobile phase.[7]

After the development is complete, the TLC plate is removed from the chamber, dried, and visualized in various ways. A common method that can help with the visibility of fluorescent compounds on the plate is UV light exposure. Another visualization technique involves using chemical reagents to enhance the visibility of the separated spots or bands, such as iodine vapours or specific staining chemicals. The distance travelled by each component is also calculated, and the Rf value can be used to distinguish between components.[7]

Visualization of compounds: A subset of electromagnetic energy called UV rays, which are located between visible light and X-rays, is a component of the electromagnetic spectrum. Compared to visible light, they are higher in frequency and shorter in wavelength. UV photons can be categorized as UVA (320–400 nanometers), UVB (280–320 nanometers), or UVC (100–280 nanometers) depending on their wavelength. UV photons can be categorized as UVA (320–400 nanometers), UVB (280–320 nanometers), or UVC (100–280 nanometers) depending on their wavelength. UV rays are employed in a wide range of fields and sectors. UV radiation has several common applications, including sterilization and disinfection, phototherapy, fluorescence and UV spectroscopy, UV curing, forensics, polymerization, and tanning. It is crucial to use UV radiation intelligently and to take the appropriate precautions. Overexposure to UV rays can be harmful to your skin, eyes, and overall health. It is advised to follow guidelines, take measures, and consult professionals while handling UV radiation or being exposed to it.[8]

IR Analysis: The term "infrared radiation" refers to the subset of electromagnetic radiation that falls between visible light and microwaves and is also known as infrared (IR) rays. They have longer wavelengths and lower frequencies than visible light. Infrared photons can generate heat when they are absorbed by substances or objects. They will be emitted by any item with a temperature higher than absolute zero (-273.15 degrees Celsius or -459.67 degrees Fahrenheit). Temperature causes a rise in the infrared radiation's intensity. Infrared photons are frequently used in many different fields because of their unique properties. Some of the main uses and applications of infrared radiation include thermal imaging, heating and energy transfer, spectroscopy, medical applications, and communication.[9]

Physiochemical Evaluation:

Organoleptic Property: In this the Organoleptic properties were studied like color, odour, appearance, etc.

Weight uniformity: Transdermal patches need to be uniform in weight since this ensures that each patch contains the same amount of the active ingredient. The consistency of a transdermal patch's weight is regularly evaluated by selecting a sample of patches and weighing each one independently.[10]

Thickness: Transdermal patches' thickness is another crucial factor because it has an impact on the rate of the active ingredient's release and the patch's efficiency. A representative sample of patches is typically selected in order to analyze the thickness of a transdermal patch, and the thickness of each patch is measured using a Vernier caliper.[11]

Folding Endurance: Folding endurance is a significant quality trait for transdermal patches since it shows the mechanical toughness and longevity of the patch. The number of failures, cracks, or breaking points that appear after folding a transdermal patch a certain number of times is a common way to gauge its capacity to fold repeatedly. How many folds the patch can withstand before breaking is used to determine its folding endurance. Although the guidelines do not provide a specific suggestion for folding endurance, it should be confirmed that the patch retains its integrity after a set number of folds.[12]

Flatness Test: Flatness is an essential component for ensuring that transdermal patches adhere to the skin properly and maintain contact with it throughout use. The patch's flatness, which is often reported as a percentage difference from a reference surface, is calculated using the thickness measurements. The recommendations in the guidelines state that transdermal patches should not deviate from a reference surface in flatness by more than 2%.[13]

Moisture uptake: The capacity of transdermal patches to absorb moisture is a critical quality aspect since it has an impact on the patch's stability and functionality. A patch may enlarge, the active substance may dissolve, or the patch's components may disintegrate as it absorbs moisture from its environment. To determine how much moisture the transdermal patches absorb, a representative sample is subjected to a controlled environment (such as a humid chamber) for a predetermined period.[14]

***In-vitro* Analysis:**

Investigations into *in-vitro* drug release were performed using the paddle over disc method. Weighed, sliced into circles, and attached to a glass plate were dry films of predefined thicknesses. The apparatus was then set to 32°C + 0.5°C, and the plate was immersed in 500 mL of pH 7.4 phosphate buffer. The paddle was then turned on and set to spin at a speed of 50 rpm with the extension set to 2.5 cm from the glass plate. The presence of drugs was then determined using a double beam UV-visible spectrophotometer at 280 nm by taking samples (5 mL aliquots) at regular intervals for up to 8 hours.[15]

RESULTS:

Phytochemical analysis: Positive results from the Mayer's Test, Ferric Chloride Test, Liebermann Test, and Killer-Killani Test all show the presence of alkaloids, phenolic compounds, steroids, and other alkaloids. However, the Steroid Test yields a negative result, indicating that Tulsi is devoid of steroids. The Ninhydrin Test also reveals the absence of amino acids. The NaOH Test and Benedict's Test, on the other hand, both show good results, proving the existence of phenols, flavonoids, and reducing sugars. Tulsi is a valuable medical herb thanks to these chemical studies, which indicate the existence of various significant phytochemical components in it.

Table 1: Results of Phytochemical analysis

Sr. No.	Name of Chemical Test	Phyto-Chemical Constituent	Observation	Result for Tulsi
1	**Mayer's Test**	For Alkaloids	Yellowish color	+
2	**Ferric Chloride Test**	For Phenolic Compounds	Violet color	+
3	**Liebermann Test**	For Steroids	Green color	+
4	**Killer-Killani Test**	For other Alkaloids like Digitalis	Bluish-green color	+
5	**Steroid Test**	For Steroids	Orange color	-
6	**Ninhydrin Test**	For Amino Acids	Purple color	-
7	**NaOH Test**	For Phenols and Flavonoids	Reddish-brown color	+
8	**Benedict's Test**	For Reducing sugars	Pale Blue color	+

Ash Values: The quantity of ash may vary depending on the source plant, the area, and the processing methods used, among other factors. Additionally, the ash readings can vary depending on the specific plant part (leaves, stems, etc.) that was tested. Here are some *Ocimum sanctum* ash values that were determined:

Table 2: Ash Values of *Ocimum sanctum*

Ash Value Type	Standard	Test
Total Ash	12% (w/w)	11.5% (w/w)
Acid-Insoluble Ash	3.2% (w/w)	3% (w/w)
Water-Soluble Ash	5.6% (w/w)	5.5% (w/w)

Extractive Values: Extractive values may differ depending on several factors, such as the plant source, geographic location, extraction method, and plant component used (leaves, stems, etc.). It is important to remember that different solvents might extract different components from *Ocimum sanctum*, and the extractive values might change accordingly. The following are *Ocimum sanctum's* calculated extractive values:

Table 3: Extractive Values of *Ocimum sanctum*

Extractive Value Type	Value
Water Extractive	21% (w/w)
Alcohol Extractive	9% (w/w)
Ether Extractive	4% (w/w)

TLC analysis: TLC was used to successfully separate the *Ocimum sanctum*. The Rf values of the divided *Ocimum sanctum* were identical to those of the original. This proved that *Ocimum sanctum* was present and in its purest form. The formula below can be used to compute it:

$$\text{Rf} = \frac{Distance\ Travelled\ by\ Solute}{Distance\ travelled\ by\ solvent} * 100$$

Rf value of (A) = 0.5

Rf value of (B) = 0.68

Rf value of (C) = 0.73

Rf value of (D) = 0.78

Rf value of (E) = 0.85

Table 4: Rf values of *Ocimum sanctum*

***Ocimum sanctum* Component**	**Standard**	**Test**
(A)	0.6	0.5
(B)	0.7	0.68
(C)	0.8	0.73
(D)	0.85	0.78
(E)	0.9	0.85

Following the use of various solvent systems for the polarity-based separation of maximum bands on TLC plates, the standard solvent system for *Ocimum sanctum* was decided to be composed of chloroform: ethyl acetate: acetic acid (50:50:1 v/v) and toluene: ethyl acetate (93:7 v/v).

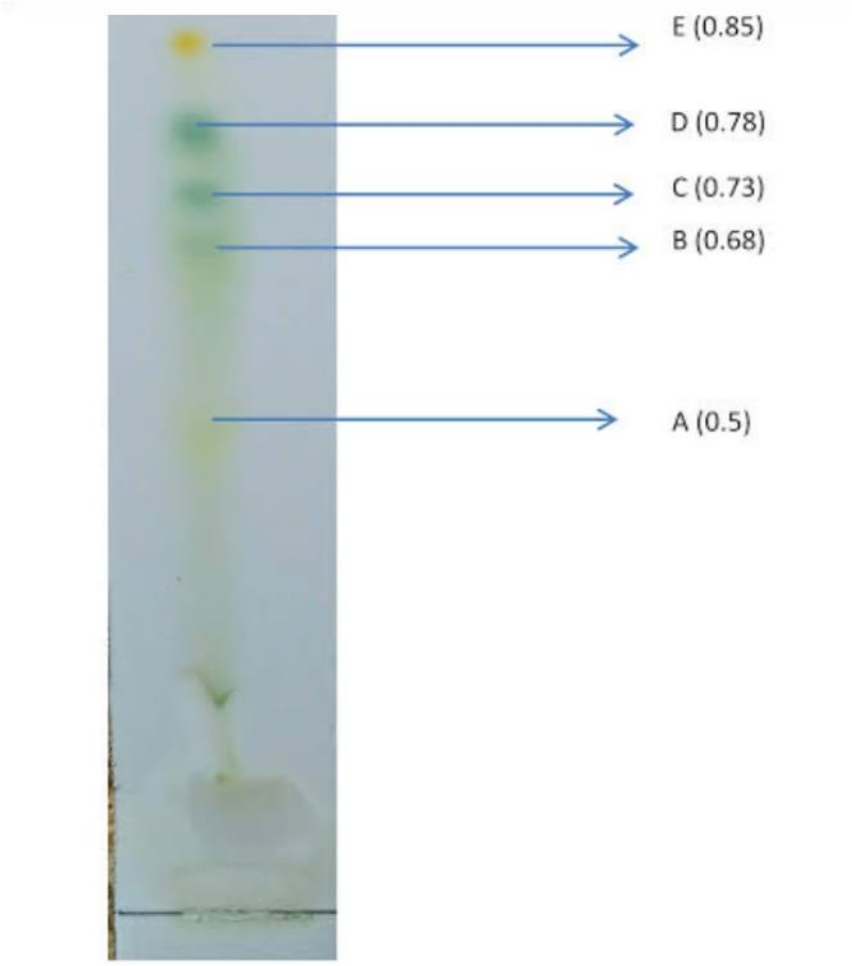

Figure 1: TLC Profile of *Ocimum sanctum*

UV analysis: Using a UV-Visible Spectrophotometer, the analytical process was straightforward, reliable, exact, and reproducible. The maximal UV absorption of each *Ocimum sanctum* was determined at a concentration of 5 g/ml.

Table No. 5: UV Absorption Maximum of *Ocimum sanctum*

***Ocimum sanctum* Component**	**UV ABS MAXIMUM (Standard)**	**UV ABS MAXIMUM (Test)**
Eugenol	282 nm	280 nm
Ursolic acid	215 nm	212 nm
Rosmarinic acid	325 nm	320 nm

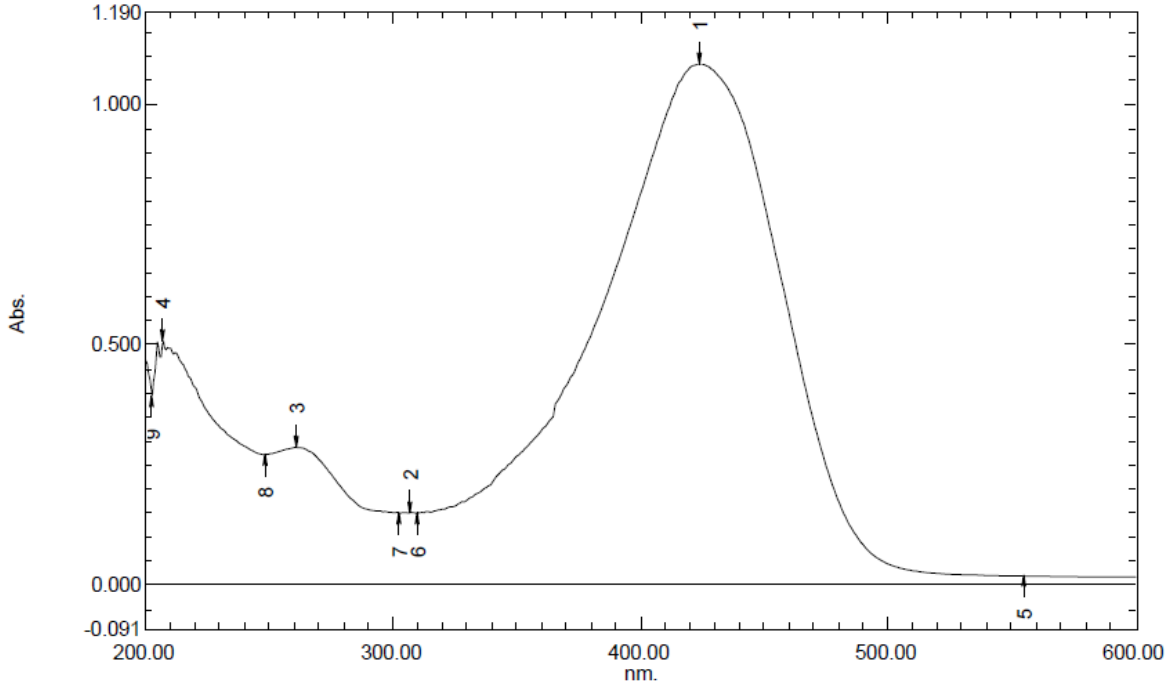

Figure 2: UV Analysis

IR analysis: It involves acquiring and analyzing a spectrum of information on chemical absorption. Functional groups can be located using IR spectroscopy.

Table No. 6: IR Analysis

Compound	Standard	Test
O-H Bending (cm^-1)	3425	3498.67
Aliphatic C-H Stretching (cm^-1)	2939	2942.22
C=C Stretching (cm^-1)	1643	1627.05
C-O Stretching (cm^-1)	1056	1204.87
C-H Bending of CH2 (cm^-1)	1485	1456.17
C-H Bending of Gem-Dimethyl group (cm^-1)	1348	1282.74
C-C Stretching (cm^-1)	1242	1204.87

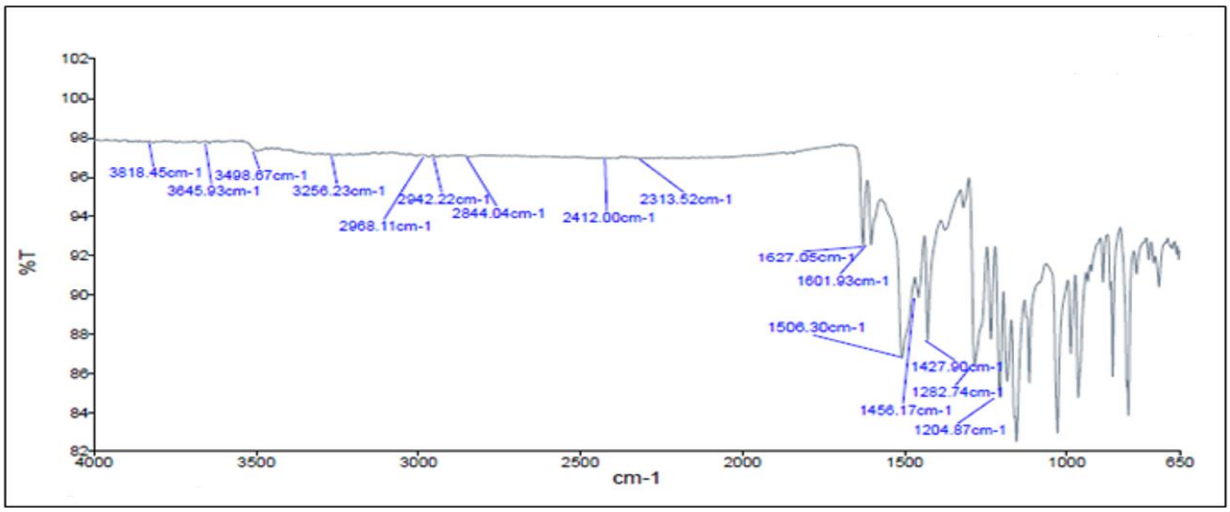

Figure 3: IR Analysis

Physiochemical analysis: Below are the results of numerous physiochemical tests:

Organoleptic Tests

Table No. 7: Organoleptic Results

Sr. No.	Characteristics	Observation
1	Colour	Whitish Cream
2	Texture	Smooth & Uniform
3	Appearance	Turbid
4	Odour	Herbal Extract

Weight uniformity Test

Table No. 8: Weight Uniformity of *Ocimum Sanctum* Transdermal Patch

Sample	Weight Uniformity ± SD
I	0.91 ± 0.0153
II	0.93 ± 0.0058
III	0.93 ± 0.0100
IV	0.96 ± 0.0152
V	0.89 ± 0.0115
VI	0.90 ± 0.0173
VII	0.94 ± 0.0208
VIII	0.93 ± 0.1528

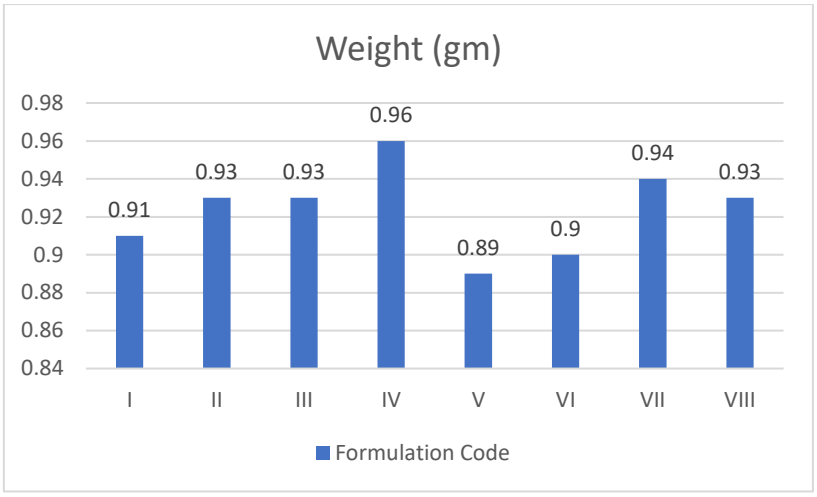

Figure 4: Weight Uniformity of *Ocimum sanctum* Transdermal Patch

Thickness Results

Table No. 9: Thickness of *Ocimum sanctum* Transdermal Patch

Sample	Thickness (mm) ± SD
I	0.35 ± 0.0115
II	0.37 ± 0.0058
III	0.36 ± 0.0153
IV	0.33 ± 0.0115
V	0.40 ± 0.0100
VI	0.39 ± 0.0058
VII	0.41 ± 0.0152
VIII	0.36 ± 0.0153

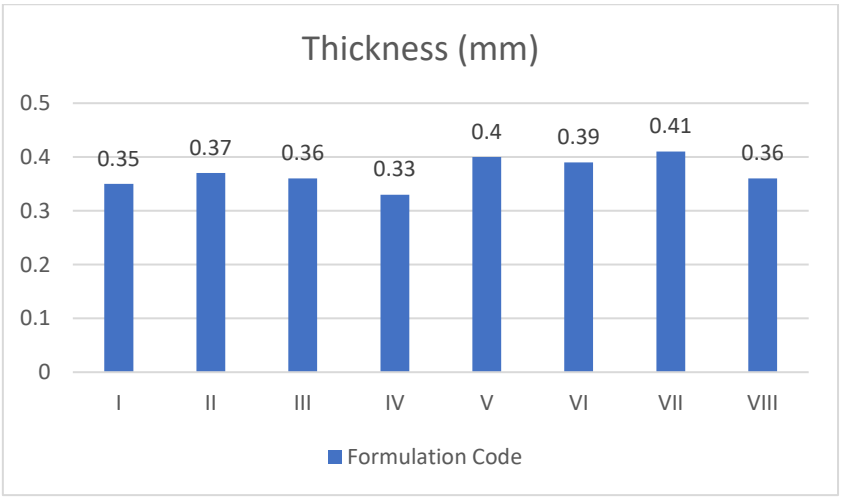

Figure 5: Thickness of *Ocimum sanctum* Transdermal Patch

Flatness Test

Table No. 10: Flatness test of *Ocimum sanctum* Transdermal Patch

Sample	Flatness % ± SD
I	94.74 ± 0.4686
II	97.43 ± 0.3143
III	88.89 ± 0.2318
IV	88.89 ± 0.2318
V	91.90 ± 0.6033
VI	94.74 ± 0.1379
VII	97.43 ± 0.3988
VIII	94.74 ± 0.1709

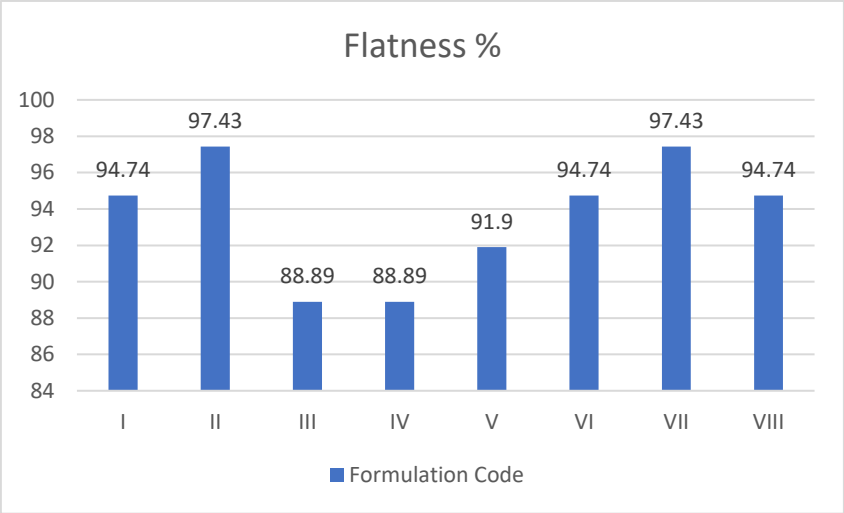

Figure 6: Flatness test of *Ocimum sanctum* Transdermal Patch

Moisture uptake

Table No. 11: Moisture Uptake of *Ocimum sanctum* Transdermal Patch

Sample	Moisture Content ± SD
I	1.695 ± 0.0145
II	2.424 ± 0.0422
III	2.312 ± 0.0200
IV	1.156 ± 0.0068
V	2.367 ± 0.0748
VI	2.941 ± 0.1175
VII	2.381 ± 0.0448
VIII	2.409 ± 0.0577

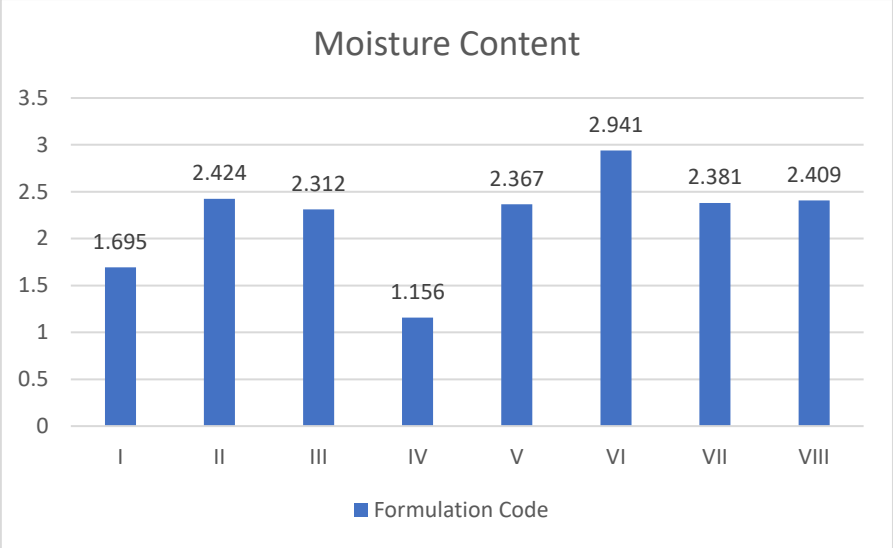

Figure 7: Moisture uptake of *Ocimum sanctum* Transdermal Patch

Folding Endurance

The created patches possessed the strength and flexibility to withstand mechanical strain, as evidenced by the folding endurance value of >150.

***In-vitro* Result:**

These results led to the selection of F1, F2, and F3 as the best formulas. All developed formulations' release characteristics were assessed *in-vitro* and contrasted. We discovered that all F3 comparison drugs have effective cumulative medication effects.

Table No. 12: *In-vitro* Drug Diffusion Study

Time (Minutes)	% Drug Diffusion		
	F1	F2	F3
0	0	0	0
30	6.78	5.2	2.98
60	10.3	8.6	4.78
90	13.65	11.21	5.64
120	17.89	15.96	7.15
150	23.1	18.54	9.45
180	29.54	22.34	14.82
210	33.68	27.45	19.38
240	39.7	31.23	25.48
270	45.58	38.42	30.98
300	48.77	43.58	38.73
330	53.22	49.86	42.54
360	57.1	55.25	45.24
390	62.41	60.46	49.64

420	67.38	65.46	53.28
450	72.34	69.46	59.74
480	77.1	73.04	64.1

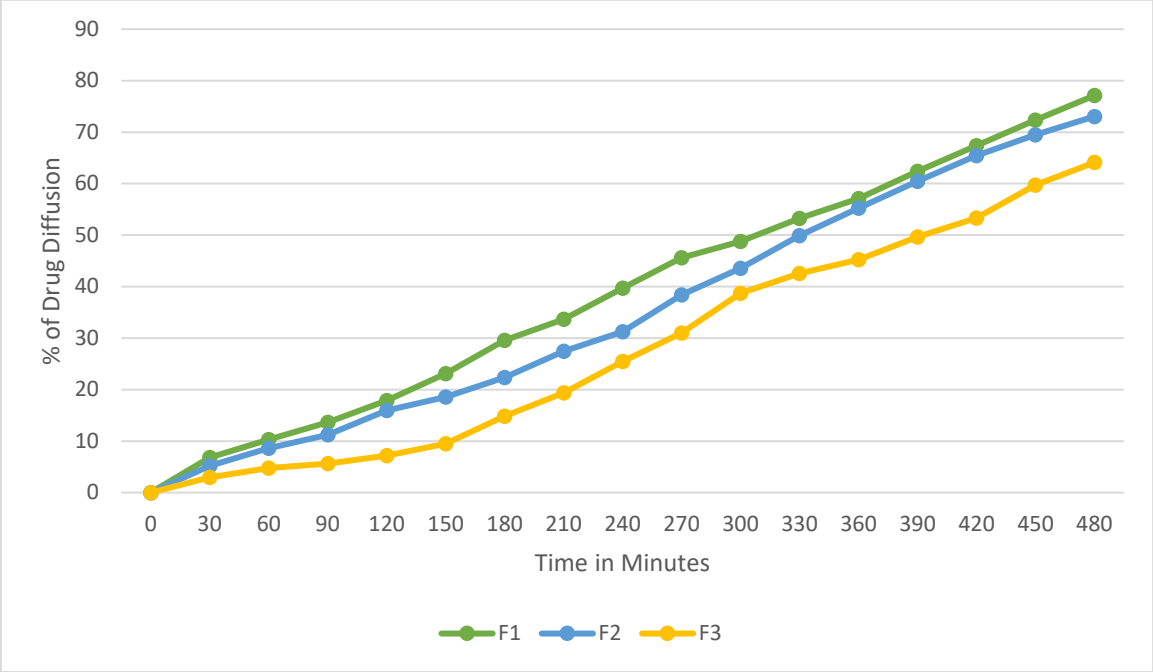

Figure 8: *In-vitro* Result

DISCUSSION: Transdermal patches are a drug delivery technology that has attracted the attention of pharmaceutical researchers due to their benefits such as regulated release, greater patient compliance, and avoidance of first-pass metabolism. The formulation design and development of a transdermal patch using *Ocimum sanctum* (Tulsi) as the active ingredient are the main topics of this thesis. Bioactive compounds such eugenol, rosmarinic acid, and ursolic acid are found in *Ocimum sanctum* and may have medicinal benefits. The purpose of this study is to develop an effective transdermal patch that can deliver these helpful chemicals exactly. To enable the efficient transportation of the medicinal chemicals through the skin, several aspects must be carefully considered during the formulation design and development of the transdermal patch employing *Ocimum sanctum*. Utilizing the therapeutic benefits of *Ocimum sanctum* while improving patient compliance, controlling drug release, and avoiding the first-pass metabolism associated with oral distribution, transdermal patches open fascinating new opportunities for drug delivery.

To successfully penetrate the skin barrier with the *Ocimum sanctum* components, various considerations must be made at the formulation design stage. This entails choosing the proper adhesive materials and matrix components for pleasant wear, picking the proper polymers for controlled release, and retaining patch flexibility. Pharmaceutical examination, which includes testing for medicine content homogeneity, thickness, weight change, and flatness, is also essential to confirming the quality and efficacy of the transdermal patch. The transdermal

patch's effectiveness, safety, and tolerance have all been confirmed by a thorough pharmaceutical investigation. *In-vitro* Analysis was performed to check further results.

The potential of *Ocimum sanctum* in numerous medicinal applications has been recognized in numerous studies. *Ocimum sanctum* extracts' antibacterial effectiveness was established demonstrating the plant's potential as a natural antibacterial agent. The plant also has anti-inflammatory, antioxidant, and immunomodulatory characteristics. In addition, *Ocimum sanctum* extracts stimulate wound healing, validating its traditional usage in treating wounds and skin diseases. Transdermal patches have also been investigated for a variety of pharmaceuticals, including antihypertensive medications, personalized medicine, and paediatric uses, and they show promise in regulated drug release and focused administration. *Ocimum sanctum* based transdermal patch development and formulation design have a lot of potential for accurate and efficient drug delivery.

CONCLUSION: With the formulation design and development of a transdermal patch using *Ocimum sanctum* as the active component, there is exciting potential for efficient drug delivery. Through a comprehensive pharmaceutical investigation that included tests for drug concentration, release profile, and skin sensitivity, the safety and effectiveness of the transdermal patch were established. These evaluations assist in the development of a safe and patient-friendly drug delivery system. Eugenol, rosmarinic acid, and ursolic acid are the bioactive substances found in *Ocimum sanctum*. As active compounds for transdermal patches, each of these shows enormous promise. Patients can benefit from *Ocimum sanctum's* anti-inflammatory, antioxidant, antibacterial, and immunomodulatory qualities, among other therapeutic effects.

New opportunities in patient care and therapy are made possible by the transdermal patch's effective formulation design and development. By utilizing the sustained release capabilities of the patch, *Ocimum sanctum* compounds can be distributed more carefully and over a longer period, potentially improving the therapeutic efficacy of the active ingredients. More research and clinical trials are needed in order to assess the therapeutic efficacy and safety of the *Ocimum sanctum* transdermal patch in practical settings. It may be possible to improve the performance of the patch by experimenting with different formulation design modifications, such as perfecting polymer pairings or looking into new permeability enhancers. While bringing contributions to the realm of transdermal drug administration, this study may improve patient outcomes.

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