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Formulation and Evaluation of Transdermal Patch of Acetyl Salicylic Acid

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Abstract
The objective of this research aimed to develop and evaluate a novel transdermal patch formulation of Acetylsalicylic acid (ASA) as an alternative to conventional oral dosage. Oral use of ASA is frequently associated with low absorption and severe gastrointestinal symptoms due to first-pass metabolism and direct mucosal irritation. To overcome these limitations, we developed a patch that incorporates ASA into a polymeric matrix, enabling controlled and extended skin release of the medication. In addition to carefully selected polymers and plasticizers that were specifically designed to maintain medication stability and ensure product uniformity, solvent evaporation methods were employed throughout the formulation process. Important physicochemical characteristics of the transdermal patches, including weight fluctuation, thickness, folding durability, moisture absorption, and drug content homogeneity, were thoroughly assessed. Permeation tests and in vitro dissolution investigations were also carried out to evaluate the medication delivery rate and release profile. According to our findings, the patches delivered a prolonged release of ASA with remarkable mechanical strength and uniformity, offering great promise for better therapeutic benefits and increased patient compliance. In addition to proving that transdermal ASA delivery is feasible, this study establishes the foundation for future investigations into other administration routes that lessen systemic adverse effects and enhance overall safety.

Keywords: *Acetylsalicylic acid, Transdermal patch, Polymer, Stratum Corneum, invitro drug release studies, Skin Permeation.*

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I. Introduction

For many years, Acetylsalicylic acid, also known as acetylsalicylic acid, has been a mainstay in the treatment of thrombosis, inflammation, and pain. The conventional oral route of administration has intrinsic drawbacks, such as high first-pass metabolism, limited bioavailability, and the risk of gastrointestinal discomfort and ulcers, despite its widespread usage. [1] These disadvantages make it necessary to investigate alternate drug delivery methods that might maximize Acetylsalicylic acid 's therapeutic advantages while reducing its negative effects. [2]

By avoiding the gastrointestinal system and hepatic metabolism, transdermal medication administration is a potential method that can minimize adverse effects and provide a regulated, prolonged release of the active pharmaceutical component. This approach makes use of the skin's accessibility and ability to carry medications straight into the bloodstream. However, because of its highly structured, lipid-rich composition, the stratum corneum the outermost layer of the skin poses a serious obstacle. Chemical penetration enhancers, physical methods like microneedles, and sophisticated vesicular carriers like ethosomes and transferosomes are some of the solutions that have been developed to overcome this obstacle. [3]Our study concentrated on creating a transdermal patch of the matrix type that incorporates acetylsalicylic acid into a polymeric framework.

Throughout the patch's shelf life, the design seeks to maintain the chemical integrity of ASA while achieving a continuous level of drug release. In-depth physicochemical analyses were carried out to evaluate variables including weight fluctuation, thickness, and folding endurance all of which are crucial elements that affect the patch's performance and stability. To replicate real-world circumstances, in vitro dissolution and permeation tests were conducted. [4] These investigations provide light on the drug's release kinetics and possible bioavailability when applied topically. This work is important because it may provide a non-invasive, safer substitute for oral Acetylsalicylic acid delivery.[5] The transdermal patch may improve patient compliance by reducing gastrointestinal exposure and facilitating continuous drug administration, especially in chronic

illnesses like cardiovascular disease where long-term, low-dose Acetylsalicylic acid treatment is crucial.[6] Furthermore, the effective creation of such a delivery system may serve as a template for other medications that encounter comparable difficulties when administered through traditional channels.[7] In addition to addressing the shortcomings of the available oral formulations, this thorough approach to transdermal system design and evaluation opens up new avenues for controlled-release technology development.[8] In the end, the research advances our knowledge of how innovative medication delivery methods might enhance treatment results and patient satisfaction.[9]

Transdermal patches of Acetylsalicylic acid are created by incorporating the medication into a polymeric matrix, allowing for sustained skin release. [10] Transdermal administration offers a number of benefits, such as preventing first-pass metabolism, guaranteeing controlled drug release, and improving patient adherence. An appropriate polymer (such PVA or HPMC) is dissolved in a solvent to create a film, which is then used to create the patch. This matrix has an equal distribution of Acetylsalicylic acid. Permeation enhancers, like DMSO, can improve medication absorption through the skin, while plasticizers, like glycerol, can be added to encourage flexibility.[11] The prepared film is cast onto a level surface and allowed to dry to form the patch.[12] Physical characteristics including thickness, weight uniformity, and flexibility are examined, together with the drug's composition, rate of release, and penetration tests conducted on Franz diffusion cells, in order to assess the transdermal patch. Testing for skin irritation and stability may also be done to make sure the patch is safe and effective for therapeutic usage. [13]

II. Material and Methods

Acetyl Salicylic Acid,HPMC,PEG 400 and Ethanol was obtained from Loba Chem PVT. LTD.

Preparation of Transdermal Patch

To prepare transparent polymeric solution, the HPMC was dissolved in ethanol. The medicine was added to this solution after the polymer had fully dissolved, and the mixture was vigorously swirled to guarantee uniform dispersion. PEG 400 was then added to the polymeric mixture to improve the finished product's stability and flexibility.[14] Then, to make it easier to remove the dried patches later, around 6 mL of the resultant solution was gently transferred into a petri dish that had been previously greased with glycerin.[15] To limit the rate of solvent evaporation and encourage homogeneous film development, an inverted funnel was put over the petri dish while the solution was allowed to dry at room temperature for a full day. After the drying process was finished, the dried patches were taken out of the petri dish and kept dry and intact until they could be examined further in a desiccator. [16]

Table-1:Formulation Table

Sr.No.	Ingredients	F1	F2	F3
1	Acetyl Salicylic Acid	100mg	100mg	100mg
2	HPMC	5gm	10gm	15gm
3	PEG 400	2.5gm	2.5gm	2.5gm
4	Ethanol	100ml	100ml	100ml

Determination of Calibration Curve (by UV 1900i Spectroscopy) [17]

The calibration curve for Acetyl Salicylic Acid was prepared by first accurately weighing 100 mg of Acetyl Salicylic Acid and dissolving it in 100 ml of phosphate buffer (PH 7.4) to prepare a 1 mg/mL stock solution. Aliquots of this stock solution were then used to prepare calibration standards by transferring 1, 2, and 3 mL into separate 10 mL volumetric flasks; each flask was then diluted to the mark with the same phosphate buffer, yielding solutions with final concentrations of 10, 20, and 30 µg/mL, respectively. These solutions were mixed thoroughly, and their absorbance was measured at 270 nm using a UV–visible spectrophotometer, with phosphate buffer serving as the blank. Finally, a calibration curve was constructed by plotting the absorbance values against the corresponding concentrations of ofloxacin, and the linearity of this curve was verified.

Solubility Study [18]

Using the saturation equilibrium technique, the solubility of the Acetyl Salicylic Acid sample was investigated. To create a supersaturated drug-in-water solution, add an excess of Acetyl Salicylic Acid in to a China dish with five milliliters of water. To evaporate the water, the China dish was placed on a water bath. To determine the dosage, a dry powder was gathered and weighed.

Melting Point Determination [19]

To estimate the melting point with the Thiele tube method, a little amount of finely powdered material is placed in a capillary tube and crushed at the closed end. The Thiele tube is then filled with liquid paraffin and securely fastened vertically. A rubber band secures a thermometer to the capillary tube, ensuring that the sample is aligned with the thermometer bulb. The assembly is submerged in liquid paraffin without contacting the glass walls. A tiny flame is given to the tube's side arm to generate convection currents, resulting in uniform heating. As the temperature rises gradually, the sample is constantly monitored. The melting point range is defined as the temperature at which the sample begins to melt and ends up totally liquefied. A small melting range shows purity, whereas a large range reveals contaminants. The experiment is repeated to ensure accuracy. This approach is extensively used since it is simple and successful at calculating melting points.

Weight Variation: [20]

Eight patches were chosen at random from the batch to be tested in order to assess weight variance. Using an analytical balance, weigh each patch separately, then note its weight. Examine each patch's weight percentage deviance in relation to pharmacopeial restrictions.

Calculating the Average Weight:

Calculate the average weight of Patches using the formula:

$$\text{Average Weight} = \frac{\text{Sum of Individual Weight}}{\text{Number of Patches}}$$

Determine the Percentage Deviation:

Calculate the percentage deviation using the formula:

$$\text{Limit} = \frac{\%\ \text{Derivation}}{100} \times \text{Average Weight}$$

Determine the Upper Limit:

Calculate the Upper Limit using the formula:

$$\text{Upper Limit} = \text{Average Weight} + \text{Limit}$$

Determine the Lower Limit:

Calculate the Lower Limit using the formula:

$$\text{Lower Limit} = \text{Average Weight} + \text{Limit}$$

Thickness: [21]

For accuracy, a Vernier caliper is used to measure the thickness of transdermal patches. Make sure the patch is clean, flat, and wrinkle-free before preparing the patch sample. Gently insert the patch between the caliper jaws after opening them just a bit wider than the anticipated thickness. Without using too much power, close your jaws until they lightly contact both sides of the patch. Take note of the reading after locking the caliper. To guarantee accuracy, take many measurements at various areas, such as the center and other arbitrary spots.

Folding Endurance: [23]

This test evaluates the patch's mechanical strength and flexibility. Cut the patch into a consistent square or rectangle shape (about 2 cm by 2 cm) to have it ready. Make sure it's wrinkle-free and smooth. To count one full fold, carefully fold the patch with tweezers in the same spot (the center) and then unfold it back to its starting position. Fold the patch repeatedly until it breaks or exhibits obvious fractures or structural damage. Calculate the average folding endurance by doing this test on a minimum of three patches from the same batch, noting the number of folds.

Folding endurance is expressed as the number of folds the patch endures before breaking or developing visible cracks.

$$\text{Folding Endurance} = \text{Number of Fold Until The Patch Breaks}$$

Moisture Uptake: [24]

Weigh each patch separately on an analytical scale to determine its initial dry weight (W_0) in order to evaluate its capacity to absorb moisture. To keep the patches at a 75% relative humidity at room temperature (25°C) for a whole day, place them in a desiccator filled with a saturated salt solution (sodium chloride). To stop moisture loss after this time, weigh the patches once more (W_1) right once. Through this test, the patch's sensitivity to humidity is assessed, along with its effects on stability, adhesiveness, and drug release.

Calculation of Moisture Uptake:

The percentage moisture uptake (MU%) is calculated using the following formula:

$$MU\% = \frac{W_1 - W_0}{W_0} \times 100$$

Where:

W_0 = Initial weight of the dried patch (before exposure to humidity)

W_1 = Final weight of the patch (after exposure to humidity)

Drug Content: [26]

Accurately weigh a section of the patch or take a specific area (i.e., 2 cm x 2 cm) to ascertain the drug content. To improve drug extraction, cut the patch into tiny pieces and put them in a volumetric flask with an appropriate solvent, such ethanol. To accomplish full extraction, sonicate the liquid or agitate it magnetically for one to two hours. To create a stock solution, dilute the solution after filtering it to get rid of the excipients. To create a calibration curve, make a standard solution with a known drug concentration at the same time. To precisely measure the drug content, use a UV spectrophotometer to measure the absorbance of the sample and reference solutions at the medication's particular wavelength (245 nm).

Acceptance Criteria:[23]

According to the Indian Pharmacopoeia, the drug content in transdermal patches should generally fall within a specified range, typically 90–110% of the labeled amount for uniformity.

Calculation of Drug Content:

Calculate the drug content using the formula:

$$\%\ \text{Drug content} = \frac{\text{Absorbance}}{\text{Total druge content in Patch (in gm)}} \times 100$$

Invitro Drug Diffusion Test: [25]

Making the receptor solution is the first step in performing an in vitro drug diffusion research utilizing a Franz diffusion cell with a transdermal patch as the membrane. To replicate physiological circumstances, fill the receptor compartment of the Franz diffusion cell with a phosphate buffer solution (PH 7.4) and keep it at 37°C. The transdermal patch should then be positioned between the donor and receptor compartments with the drug-releasing side toward the receptor solution after being trimmed to match the cell's diffusion area, which is usually about 1.5 cm^2. Lock up the compartments to stop leaks. To guarantee temperature stabilization and adequate patch hydration, let the system equilibrate for about an hour. To reduce contamination and evaporation, cover the donor compartment with aluminum foil before starting the diffusion investigation. Use a magnetic stirrer to continuously mix the receptor solution at a constant speed, such 120 rpm, to ensure uniform concentration. Using a syringe, remove a specified amount (5 mL) of the receptor solution at predefined intervals (e.g., 0.25, 0.75, 1.25, 1.75, 2.25, and 4 hours) and promptly replace it with an equivalent volume of freshly
warmed phosphate buffer to ensure consistent volume and sink conditions. To find the drug concentration, use a UV spectrophotometer to analyze the samples that were obtained. To get the permeation profile, compute the total amount of medication that has penetrated per unit area at each time point and plot this against time. Calculate the permeation flux, which gives information on how quickly the medication diffuses through the transdermal patch, from the linear part of this curve. Using a Franz diffusion cell, this technique provides a systematic way to assess the drug release and penetration properties of transdermal patches.

III. Resultsand Discussion:

1. Calibration Curve

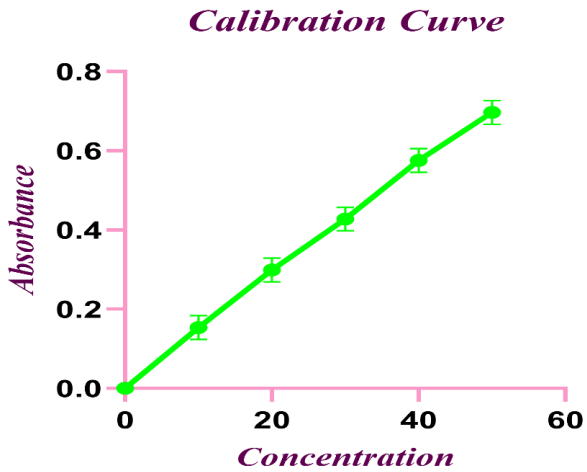

Fig.1 Calibration curve of Acetyl Salicylic Acid.

Solubility Study

Table-2: Result of Solubility test

Sr.No.	Solvent	Solubility
1	Water	Slightly Soluble
2	Ethanol	Soluble
3	DMSO	Soluble
4	Acetone	Soluble
5	Methanol	Soluble

Melting Point

Using a Thiele tube technique, the Acetylsalicylic acid sample's melting point was discovered to be 134±0.5°C. This result validates the identification and purity of the synthesized chemical by falling within the stated range of 134–136°C.

Table-3: Physical Characterization.

Formulation	Weight Variation (gm)	Thickness (mm)	Folding Endurance
F1	1.32±1.2	0.346	142
F2	1.38±1.1	0.352	143
F3	1.32±1.1	0.349	142

Moisture Uptake

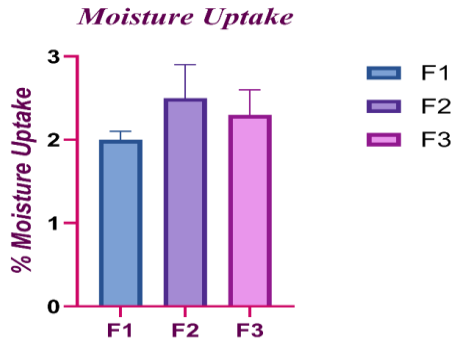

Fig.2 Moisture Uptake of Acetyl Salicylic Acid.

Drug Content [22]

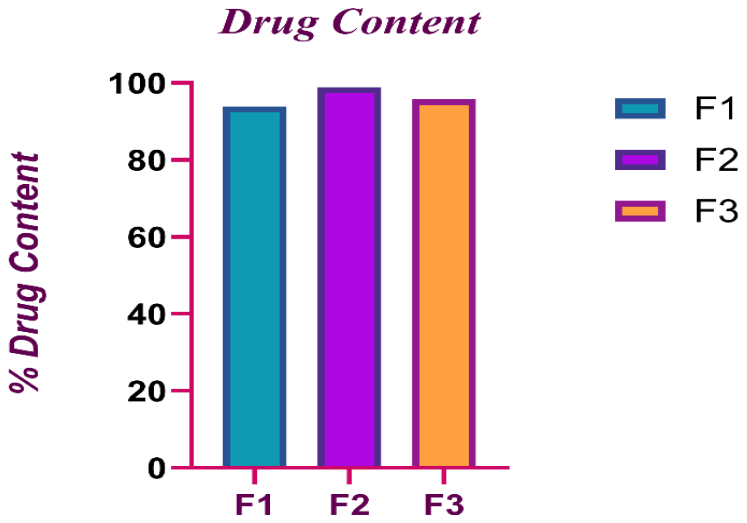

Fig.3 Drug Content of Acetyl Salicylic Acid

Invitro Drug Release Studies

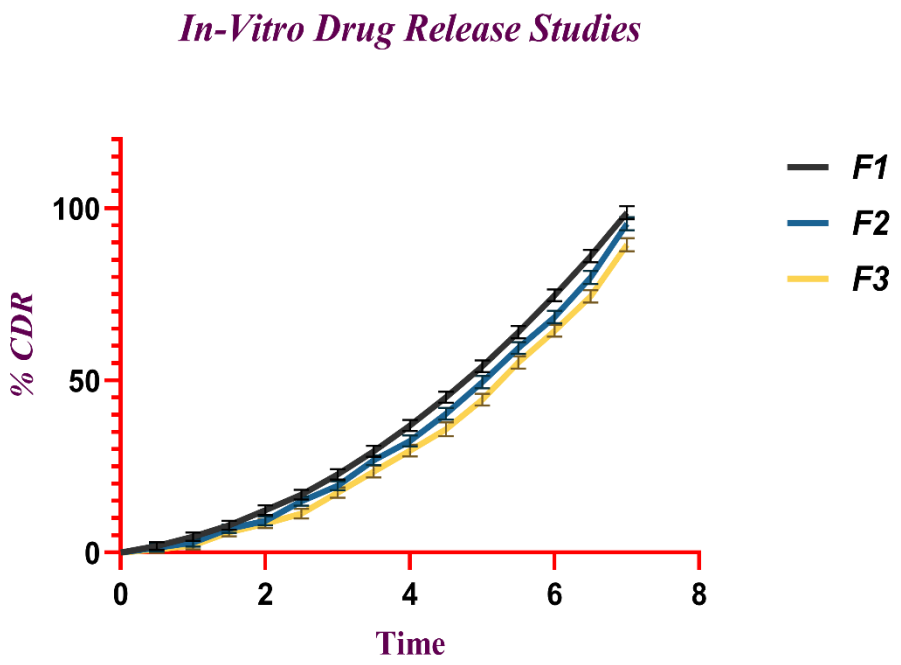

Fig.3 Invitro Drug release studies of Acetyl Salicylic Acid

IV. Summary:

Acetylsalicylic acid transdermal patches have been successfully prepared using the solvent evaporation approach. The method used to formulate the transdermal patches was reproducible and guaranteed exceptional quality and uniformity in patch characteristics with the least amount of variability, according to an evaluation of the prepared patches in terms of organoleptic, weight, thickness, moisture content, and drug content uniformity. In this study, the solvent casting process was used to synthesize and assess TDDS for sustained release ASA.

To encourage the transdermal transport of the active ingredient, transdermal patches were developed. In order to guarantee the appropriate transdermal dose form, we set out to identify the ideal production conditions for transdermal patches using polymer in our series of tests. It has been demonstrated that the suggested analytical approach is straightforward, precise, and meets all validation requirements. The solubility and meting point test shows that the results does not show any significant changes. The folding capacity of prepared patch is flexible and maximum drug content has been observed in F2 formulation. According to stability studies, there is no discernible variation in the transdermal patch's drug release rate.After 30 days at ambient temperature and humidity, the most optimal formulation F2 was determined to have a 97.02% success rate.

The patch was confirmed to be compatible with skin since skin irritation examinations did not reveal any signs of erythema or any other skin irritation reaction. This suggests that neither the medicine nor any polymer or excipient had any negative effects on the skin. All assessment parameters yielded good results within acceptable bounds. Based on the results the F2 formulation shows better and optimized results when compared to F1 and F2.

The patch provided a continuous and controlled release of acetylsalicylic acid, ensuring a constant medicine concentration and reduced moisture absorption, according to in vitro evaluations that included dissolving and penetration tests. Transdermal Acetylsalicylic acid delivery seems to be a feasible and promising alternative that might improve treatment outcomes and patient compliance by bypassing first-pass metabolism and reducing gastrointestinal side effects. Future research is recommended to further optimize the formulation and validate therapeutic efficacy through extended in vivo experiments.

V. Conclusion:

The study demonstrated that creating a transdermal patch might successfully solve the limitations of conventional oral acetylsalicylic acid delivery. The generated patch exhibited consistent physical characteristics, such as optimal thickness, uniform weight, and remarkable folding endurance, and was based on a polymeric matrix of carefully selected polymers and plasticizers.

The patch provided a continuous and controlled release of acetylsalicylic acid, ensuring a constant medicine concentration and reduced moisture absorption, according to in vitro evaluations that included dissolving and penetration tests. Transdermal Acetylsalicylic acid delivery seems to be a feasible and promising alternative that might improve treatment outcomes and patient compliance by bypassing first-pass metabolism and reducing gastrointestinal side effects. Future research should focus on further formulation optimization and clinical efficacy confirmation through extended in vivo experiments.

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