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Novel Transdermal Patch: Bindi for Women to Treat Migraine

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ABSTRACT

Transdermal patches have emerged as a promising delivery system for the effective treatment of migraine, with innovations like 'Ladies Bindi' paving the way for more convenient and patient-friendly therapeutic options. Traditionally physicians prescribe Sumatripton, Ergotamine, Caffaine tablet to treat migraine. According to national headache foundation most of the females are affected by migraine headache. Sumatripton, Ergotamine used for transdermal topical applications. Instead of traditional transdermal patches, we have developed a TDDS in the form of 'Ladies Bindi' this innovative approach not only enhances patient compliance but also provides a discreet and non-intrusive methods of medication administration, allowing women to seamlessly combine the benefits of Bindi with therapeutic advantages of a transdermal patch. Due to significant hepatic first-pass metabolism, just approximately 95% of the administered dose enters the systematic circulation. This underscores the imperative for exploring routes of drug administration for such compounds. Sumatriptan has 100% transdermal bioavailability, the objective of this study was to formulate diverse transdermal matrix film using various ratios of hydrophilic and hydrophilic-lipophilic combinations, incorporating Sumatriptan as the active ingredient. We conducted comprehensive physicochemical and in vitro evaluations, as well as primary irritation studies on the developed film. This research aims to establish a controlled and sustained drug delivery system trough intact skin, enabling the maintenance of therapeutically effective drug level for an extended period using 'Ladies Bindi'.

INTRODUCTION:

Sumatriptan is a serotonin receptor agonist, mainly used to treat migraines and cluster headaches. Nowadays recent technological advancement in transdermal delivery is the use of electrical potential to promote a medication's movement through the skin. In this research transdermal film of Sumatriptan were formulated by using different polymer combinations such as ethyl alcohol,polyethyleneglycol600,Span20, oleic acid, bisabolol, cineole, limonene, plastoid E 35H, sorbitol; for the evaluation of the content of the formulation we used different methods like diffusion cell, different physicochemical properties, surface area, drug release pattern and percentage of drug released used to check plasticizers, sumatriptan film, hydrophilic and hydrophobic polymer layer or combination of hydrophilic and hydrophobic polymer. We checked release pattern of the drug and rate kinetic and found that this patch is following zero order kinetic. This non-irritant patch offers valuable added advantage, such as consistency in drug release, reduced dosing frequency, easy to apply, look pretty and fulfilled patient compliance.

Material and Methods:

All chemicals were procured from local vendors Omkar Traders and Sahyadri Chemicals. All Chemicals are of laboratory and analytical grade.

Table 1.: List of Chemicals

Sr. No.	Name of the Ingredients	Category	Supplier
1	Sumatriptan succinate	Drugs	Omkar Traders
2	Polyvinyl alcohol	Polymer	Omkar Traders
3	Polyvinyl pyrrolidone	Polymer	Sahyadri Chemicals
4	Ethylcellulose	Polymer	Sahyadri Chemicals
5	Dibutyl phthalate	Plasticizer	Sahyadri Chemicals
6	Propylene glycol	Plasticizer	Sahyadri Chemicals
7	Backing membrane	Bindi	Local Market Shop

Methods:

Preparation of Patch: The film was fabricated using the film casting methods, employing specially designed glass molds in conjunction with transparent plastic sheets as backing membrane. Diverse polymer combinations, including PVA:PVP and EC:PVP, were employed in the film preparation process. Different ratios of polymers within each pair were dissolved using distinct solvents, namely water and chloroform. The ultimate concentration of the polymer blend in each solution was standardized to 4% to 10% for different formulations. The solutions were formulated at ambient room temperature, incorporating plasticizers at a ratio of 20% DBP for EC:PVP combination and 20% propylene glycol for the PVA:PVP combination. The drug was integrated into a 10% polymer solution, achieved through stirring on a magnetic stirrer. The polymer solution was poured into a glass mold, with solvent evaporation rates regulated through the use of an inverted cup funnel. Following a 24-hr period, the dried film was carefully removed and stored in desiccators for further use.

Table2:List of Instrument

Sr. No.	Name	Model / Manufacturer
1	Analytical weighing balance	Wensar **Manufacturer**
2	UV spectrophotometer	Lab India-2700
3	Magnetic Stirrer	BR instrument
4	Sonicator	BR Instrument
5	Hot Air Oven	Lab hosp
6	USP Dissolution Apparatus	Lab India
7	Digital PH meter	Equiptronics
8	Stability chamber	BR Instrument
9	Franz Diffusion Apparatus	BR Instrument

Table 3: Formulation of transdermal patch in the form of Bindi

Batch No.	Polymer %w/v	Plasticizer %w/v	Drug per Batch	Solvent system (Water :Chloroform)(6:4)(ml)
	EC:PVP	DBP		
1	10:0	20	10	10ml
2	9:1	20	10	10ml
3	8:2	20	10	10ml
4	7:3	20	10	10ml
5	6:4	20	10	10ml

	PVA:PVP	PG		
6	10:0	20	10	10ml
7	8:2	20	10	10ml
8	6:4	20	10	10ml
9	4:6	20	10	10ml
10	2:8	20	10	10ml

Physical evaluation of Medicated Patch

Physical Appearance

All the films that were prepared underwent a visual inspection to access characteristics such as color, transparency, surface texture and flexibility to determine their quality and effectiveness.

Thickness and Weight variation Study

The width of the patches was measured at different intervals using micrometer, and the average value was calculated. A small film strip with different dimensions resembles to ladies bindi were used for this purpose. Also to determine tensile strength the film was pulled through the pulley system and amount of force was calculated.

Solubility and Drug Content Examination

The solubility of triptans was checked in determinant pH buffer for different time intervals of 1 to 12 hrs. We are selected metal halide phosphate buffer with pH 7.4. Selected few patches were crushed and mixed in said solution; filtered; scanned at 244nm wavelength in a spectrophotometer.

Swelling and Erosion

Swelling and Erosion of patches were determined under conditions identical to those for dissolution tests. The degree of swelling (Water uptake) and extent of erosion (mass loss) were determined according to the equations:

Degree of swelling = Wet weight - Original dry weight

Original dry weight

% Erosion = Original weight – Remaining dry Weight × 100

Original weight

Folding Endurance

The folding endurance of the patch is essential to study the elasticity of the film during handling. This can be done by repeatedly folding one film at the same place till it break. A multiple determinations were performed in triplicate.

Content Uniformity

For this examination, patches with an area1cm^2 were taken into small and equal pieces, and then transferred into 50ml phosphate buffer having 7.4 and kept into constant shaker. With one hr interval filtered extract was taken, made appropriate dilutions and assayed by UV-Spectrometric technique.

pH of the Surface

To check pH of the surface we used phosphate buffer of pH 7.4. After one hr. interval pH was checked by using digital pH meter, close to the surface of the patch.

***In-Vitro* release study of Sumatriptan**

For the drug release study dissolution apparatus is used. For this study 100 ml phosphate buffer (pH 7.4) were used as a dissolution medium. Temperature was kept at 36.7^{o}C. Speed was set at 50RPM. After 30min of intervals small faction were collected till8hrs. these factions were filtered and diluted with distilled water and analyzed at 280nm by using UV-Spectrophotometer. We repeated this process for three times.

In-Vitro Permeability

A healthy mature mice was taken, sacrificed with diethyl ether, hairs from dorsal region were shaved carefully. Hairless skin was removed with the help of surgical scissors. The skin was carefully detached from animal after incision. After preparation of the mice skin Franz diffusion cell was filled with phosphate buffer (pH 7.4) and temperature was maintained at

37.0 ^{0}C throughout procedure. Skin was placed over the open end of the receptor compartment. Then prepared sample Bindi were placed on to the skin. The donor compartment is placed over the receptor compartment and holds this compartment with clamp. Sample were collected each 30min interval and analyzed under UV-Spectrophotomete.

Assay of Patch

A complete patch from the petri plate was cut in to2*2 pieces and crushed in mortar pestle and dissolved in phosphate buffer pH 7.4 with continuous agitation. Then contents were filtered through Whatman filter paper into volumetric flask. After appropriate dilution with phosphate buffer pH 7.4, solutions were analyzed by determination of absorbance at 226nm (UV 2450 spectrophotometer) against a solvent blank. Drug content was estimated from a calibration curve.

Result and Discussion

The transport of drug molecules across the skin is a crucial yet intricate stage in the development of transdermal drug delivery systems. Overcoming this challenge requires the application of various methods and techniques, with the use of penetration enhancers being a notable approach. The primary objective of the current investigation was to develop, design, formulate, and assess transdermal patches in the form of Bindi containing Sumatriptan Succinate. These patches incorporated PVA:PVP and EC:PVP as penetration enhancers, aiming to improve the permeation and transport of the drug through the skin. Considering the limited permeability of DS (drug substance), a monolithic drug delivery device has been explored. Placebo films were examined for their flexibility, clarity, elasticity, and ease of removal from molds. Additionally, assessments were conducted for thickness uniformity, percentage flatness, moisture uptake, tensile strength, modulus of elasticity, and percentage elongation at break. Both placebo and medicated transdermal films exhibited 98-100% flatness, indicating no significant constriction. Consequently, these formulations are capable of maintaining a smooth and uniform surface when applied to the skin.

No signs of erythema or edema were observed on the skin of human volunteers, except for a mild response elicited by the patch containing a lipophilic polymer after 24 hours of film application. The findings from the aforementioned studies lead to the conclusion that polymeric matrix-type transdermal films of D, formulated with various grades and ratios of

polymers, exhibit potential for transdermal delivery. The drug release profile over time demonstrates a linear and slow controlled pattern, further supporting the suitability of the test products for transdermal films. While the developed formulation showcases the most effective combination of polymers, slight modifications are needed to achieve therapeutic plasma concentration.

Conclusion

Transdermal drug delivery, which means delivering medicine through the skin, is a well-known way to give medication. It has many advantages compared to older methods like swallowing pills. For example, it avoids the stomach and intestines, which can sometimes cause problems. Also, it can give the medicine slowly and steadily over time, which can be helpful for some conditions. People might find it easier because they don't have to remember to take pills or deal with needles. One common medicine for migraines is sumatriptan. New research suggests that a special patch called Zelrix, which uses a method called iontophoresis, might offer another choice for treating migraines.

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Conflict of Interest: Authors do not have conflict of interest in given manuscript.

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