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FORMULATION AND EVALUATION OF TRANSDERMAL PATCHES CONTAINING GRISEOFULVIN

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Abstract:
Griseofulvin, an antifungal agent, is a BCS class II drug slowly, erratically, and incompletely absorbed from the gastrointestinal tract in humans. The clinical failure of the conventional oral therapy of griseofulvin is most likely attributed to its poor solubility and appreciable inter- and intra-subject variation in bioavailability from different commercial products. Moreover, the conventional oral therapy is associated with numerous adverse effects and interactions with other drugs. In the proposed research work, we are wanting to get ready transdermal patches of an antifungal drug Griseofulvin with the accompanying goal. Transdermal patches stacked with Griseofulvin will be arranged involving polymers in changing focus by dissolvable vanishing strategy.The pre-arranged transdermal patches will be assessed for different boundaries like weight variety, thickness, collapsing perseverance, drug content, level of dampness content, in-vitro drug release study

Key words: *Griseofulvin, transdermal patches, Formulation, Evaluation*

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INTRODUCTION:

Controlled release medication may be defined as the permeation-moderated transfer of an active material from a reservoir to a target surface to maintain a predetermined concentration or emission level for a specified period of time. Transdermal drug delivery system can be defined as the controlled release of drugs through intact skin. Controlled release technology has received increasing attention in the face of a growing awareness that substances are frequently toxic and sometimes ineffective when administered or applied by conventional means. The transdermal course currently positions with oral treatment as the best imaginative exploration region in drug conveyance, with around 40 % of the medication conveyance up-and-comer items under clinical assessment connected with transdermal or dermal framework [1].

A transdermal fix is a cured glue fix put on skin to convey a period delivered portion of prescription through the skinfor treating effective or deliberate ailment. Since mid.1990, this dose type of transdermal helpful framework has been accessiblein the drug market.1 Aongoing way to deal with drug conveyance is to convey the medication into fundamental flow at foreordained rateinvolving skin as a site of utilization. A transdermal medication conveyance is a detailing or gadget that keeps up with the blood centralization of thedrug inside helpful window guaranteeing that medication levels neither fall underneath the base compelling focus nor surpassleast harmful dose.2 Such a framework offers assortment of critical clinical advantages over different frameworks, like tablet and infusions. For instance, it gives controlled arrival of the medication and produces a consistent blood-level profile prompting diminished foundational secondary effects and, once in a while, further developed viability over other measurements structure. Inaddition transdermal dosage form is user-friendly, convenient, painless, and offers multi-day dosing, it generally leads to improved patient compliance.[3] It offers many important advantages over oral drug delivery, e.g., gastrointestinal and hepatic first pass metabolism, reduces variation in delivery rates, avoids interference due to presence of food, controls absorption rate, suitable for unconscious patients, and enables fast termination of drug delivery, if needed [2].

Basically, not every drug or chemical is a candidate for transdermal drug delivery. The decision of medication is the main choice in the effective improvement of a transdermal item. The main medication properties that influence its dissemination through the gadgets as well asthe skin incorporate atomic weight, compound usefulness and liquefying point.It is by and large acknowledged that the best medication contender for aloof glue transdermal patches should be nonionic, low atomic weight (under 500 Daltons), have satisfactory solvency in oil and water (log P in the scope of 1to 3), a low melting point (less than 200 ℃), short plasma half-life, and are potent (dose is less than 50 mg per day, and ideally less than 10 mg per day). Given these operating parameters, the number of drug candidates for passive transdermal patches is low, owing to the challenge of diffusing across the bilayers in the tortuous stratum corneum. But, many new opportunities still exist for novel passive transdermal patch products. The new transdermal technologies that were introduced in the previous section challenge the paradigm that there are only a few drug candidates for transdermal drug delivery. With the active and micropore-creating transdermal technologies, molecular size is not a limiting factor. The same applies for other physiochemical drug properties, such as ionization state, melting point, and solubility. Finally, the active and micropore-creating technologies also enable therapeutic delivery of drugs at doses higher than 10 mg. Clearly, the opportunities for transdermal drug delivery have been greatly expanded through the application of new formulation technologies and active delivery systems. Now, a much wider set of drug compounds, including macromolecules, have the possibility to be delivered transdermally at therapeutic levels than was possible just a decade ago. Of course, the use of a TDD technology for any drug must be clinically beneficial [3].

As of late, different medication conveyance frameworks have been created which give supported discharge treatment by means of a sub-dermal supplement. Frameworks have been unveiled which likewise give drug conveyance frameworks appropriate to transdermal medication organization. A large number of the antihistaminic drugs have the properties important to be successful in a transdermal medication conveyance framework. The properties incorporate high power, legitimate physic-substance qualities, great dermal entrance and absence of dermal bothering [4].

In the proposed research work, we are wanting to get ready transdermal patches of an antifungal drug Griseofulvin with the accompanying goal. Transdermal patches stacked with Griseofulvin will be arranged involving polymers in changing focus by

dissolvable vanishing strategy. The pre-arranged transdermal patches will be assessed for different boundaries like weight variety, thickness, collapsing perseverance, drug content, level of dampness content, in-vitro drug release study and so on. The fix is supposed to conveyance griseofulvin at consistent rate and for delayed span for treatment of shallow contagious diseases. A lower transdermal portion of the medication would be expected for accomplishing wanted remedial activity when contrasted with oral organization.

MATERIAL AND METHODS:

Preparation of Transdermal Patches

The matrix transdermal patches containing griseofulvin changed into prepared via solvent evaporation approach using one-of-a-kind ratios of HPMC and ethyl cellulose. The backing layer became casted by way of pouring four% PVA solution within the petri-plates coated with aluminum foil, observed by using drying at 60ºC for three-four h in hot air oven.

In the technique of components, to begin with, the polymer (HPMC) become taken in a beaker with a solvent dichloromethane: methanol (2:1) and was allowed to completely swell for a length of 1 hour. Subsequently, with constantly stirring, ethyl cellulose changed into brought. Afterward, the plasticizer (PEG four hundred) and permeation enhancer (SLS) had been added and mixed uniformly for the couple of minutes length. Finally, the drug become incorporated with non-stop stirring to mix properly. The resultant homogenous dispersion become unfold over a backing membrane. Later, the controlled solvent evaporation changed into executed by means of heating and the fabricated dried film changed into cut into 10 cm2 size. The prepared films have been wrapped in aluminum foil and saved within the desiccator for in addition examine. Table 1 describes the composition in formulating the transdermal patches[5].

Table 1: Composition of Transdermal patch formulations

F. Code	Ratio of polymer (EC: HPMC)	Total wt. of Polymers (mg)	Solvent(DCM:Methanol, 2:1) (ml)	Plasticizer (PEG-400) (mg)	Permeation enhancer (SLS) (mg)	Griseofulvin (mg)
GTP1	8.5:1.5	1000	30	200	80	100
GTP2	7:3	1000	30	200	80	100
GTP3	6:4	1000	30	200	80	100
GTP4	4:6	1000	30	200	80	100
GTP5	3:7	1000	30	200	80	100
GTP6	1.5:8.5	1000	30	200	80	100

Evaluation of Transdermal Patches

Small patches of 2.54 cm^2 area were cut from the stored films and the evaluation of various parameters was carried out on the patches [6-9].

Weight Variation

The patches were subjected to mass variation by individually weighing randomly selected patches. Such determinations were carried out for each formulation.

Thickness

The thickness of each patch was measured by using screw gauge at different positions of the patch and the average was calculated.

Folding endurance

Folding endurance was determined by repeatedly folding one patch from the same place till it broke. The number of times the film could be folded from the same place without breaking/ cracking gave the value of folding endurance.

Percentage moisture content

The prepared transdermal films were weighed individually and kept in desiccators containing fused calcium chloride at room temperature for the duration of 24 hours. After 24 hours, the films were re-weighed and the percentage moisture content was determined by the given formula

Percentage of moisture content = Initial weight – Final weight/Initial weightx 100

Drug content determination

For determining the drug content, an area of 10 cm^2 of the patch was cut and dissolved in 10 ml of phosphate buffer (pH 7.4). After that, 0.1 ml volume was withdrawn from the solution and diluted with the phosphate buffer to 10 ml in a volumetric flask. The absorbance of the solutionwas taken at 295 nm by using UV spectrophotometer.

***In-Vitro* Permeation Study**

In-vitro permeation studies of the patches have been carried out with the aid of the use of Franz diffusion cell with a receptor compartment capacity of 60 ml. The formulated patch of surface area of zero.Sixty four cm2 changed into positioned in among the dialysis membrane and the donor compartment and then dialysis membrane turned into established between the donor and receptor compartment of diffusion cell. The receptor compartment of diffusion mobile was filled with phosphate buffer saline pH 7.Four. The complete meeting turn out to be regular on a magnetic stirrer and the solution in the receptor compartment changed into constantly and constantly stirred magnetic beads at 50 rpm; the temperature was maintained at 37±zero.5ºC.The 1 ml aliquots had been withdrawal at extraordinary time periods (0, 1, 2, 3, 4, 6 and 24 h) and analyzed the drug content with the aid of UV at 295 nm.The receptor section modified into replenished with an identical volume of phosphate buffer (37ºC) at every sample withdrawal, the cumulative quantity of drug permeated in keeping with square centimeter of patches have been plotted in competition to time. Percent drug permeated and log % DRP become calculated and tabulated.

RESULTS AND DISCUSSION:

Evaluation of transdermal patches

The common weight of the patches changed into determined to be starting from 123 to 158 mg. The thickness of the patches ranged from 0.239 to 0.319 mm and was located to be depending on the polymer ratio.

The patches were able to face up to 39 to 73 folds at equal area in the folding endurance test. All the formulations were able to included uniform quantity of drug in them starting from 98.Three to 99.2 %. The outcomes of moisture content material examine discovered that increase in concentration of HPMC become at once proportional to the moisture content material within the patches with GTP6 showing the best moisture (7.08%) even as GTP1 exhibiting the bottom (5.17%). The drug becomes released ranging from 87.3 to 59.7% in numerous formulations. The regression coefficients of the graphical illustration of the mathematical fashions display that the discharge of griseofulvin from the patches can be described via Korsemeyer-Peppas model. The expression relates that the drug released from the patches is due to diffusion of drug from the polymeric matrix of the patch and is more often than not diffusion managed.

Table 2: Physiochemical features of Transdermal Patches

	Thickness (mm)	Average weight (mg)	Moisture content (%)	Drug content (%)	Folding Endurance
GTP1	0.239	152	5.17	98.3	39
GTP2	0.251	158	6.31	99.2	43
GTP3	0.264	136	6.43	98.35	43
GTP4	0.295	123	6.58	98.18	51
GTP5	0.297	127	6.96	99.16	63
GTP6	0.319	135	7.08	98.18	73

Table 3: Release data of Griseofulvin from patch

Time (h)	1	2	3	4	6	24
GTP1	5.17	14.18	21.24	42.68	69.18	87.3
GTP2	4.94	13.88	21.01	40.19	61.15	76.8
GTP3	4.33	11.45	19.18	43.85	58.96	65.1
GTP4	5.08	14.07	20.58	41.16	64.25	65.2
GTP5	4.86	12.18	17.68	40.58	61.04	63.6
GTP6	2.94	10.58	18.34	38.81	54.11	59.7

Table 4: Statistical data of kinetic modeling of drug release from patch

	Zero Order		First Order		Higuchi		Korsemeyer-Peppas	
	Slope	**R^2**	**Slope**	**R^2**	**Slope**	**R^2**	**Slope**	**R^2**
GTP1	3.143	0.696	-0.036	0.876	21.27	0.819	0.903	0.842
GTP2	2.7	0.685	-0.024	0.821	18.35	0.814	0.868	0.834
GTP3	2.195	0.548	-0.016	0.626	15.39	0.693	0.87	0.78
GTP4	2.151	0.519	-0.016	0.557	15.2	0.666	0.813	0.78
GTP5	2.412	0.532	-0.016	0.58	15.05	0.675	0.835	0.786
GTP6	2.03	0.555	-0.014	0.622	14.23	0.702	0.937	0.766

CONCLUSION:

The common weight of the patches changed into determined to be starting from 123 to 158 mg. The thickness of the patches ranged from 0.239 to 0.319 mm and was located to be depending on the polymer ratio. The patches were able to face up to 39 to 73 folds at equal area in the folding endurance test. All the formulations were able to included uniform quantity of drug in them starting from 98.Three to 99.2%. The outcomes of moisture content material examine discovered that increase in concentration of HPMC become at once proportional to the moisture content material within the patches with GTP6 showing the best moisture (7.08%) even as GTP1 exhibiting the bottom (5.17%). The drug becomes released ranging from 87.Three to 59.7 % in numerous formulations. The regression coefficients of the graphical illustration of the mathematical fashions display that the discharge of griseofulvin from the patches can be described via Korsemeyer-Peppas model. The expression relates that the drug released from the patches is due to diffusion of drug from the polymeric matrix of the patch and is more often than not diffusion managed.

Griseofulvin exhibits amazing capability for administration through transdermal path for the remedy of neurological situations. The objective of the existing investigation turned into to assess the transdermal movies of griseofulvin to its applicability to lessen the dose of the drug. It may be concluded that transdermal drug delivery system of griseofulvin can be formulated, which presents better compliance than conventional drug transport gadget due to decreased dose and prolonged launch of the drug. The patch formula of griseofulvin can be of unique advantage for topical treatment of fungal infections.

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