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Formulation Development And Evaluation Of Terbinafine Using Quality By Design Approach

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ABSTRACT:

Terbinafine is an antifungal allylamine that is commonly used to treat infections caused by dermatophytes (Trichophyton, Epidermophyton, and Microspora), such as tinea infections. Terbinafine works by inhibiting the enzyme squalene epoxidase in fungal ergosterol biosynthesis, resulting in intracellular squalene accumulation and cell death. For seven sample batches, microcrystalline cellulose, sodium starch glycolate, hydroxyl propyl methylcellulose, magnesium stearate, and colloidal silicon dioxide were used in various quantities and compositions. The photostability study looked into the medicine excipient compatibility. In the photostability research, no significant alterations were found. The tablets were tested for disintegration, consistency of content, and friability. Drug release profile in vitro, Scale-up and large-scale manufacturing, as well as a validation process, may be created in the future for marketing approval.

Keywords: Drug, Process, Tablets, Scale, Fungal.

INTRODUCTION:

Terbinafine is an allylamine antifungal drug used to treat onychomycosis, tinea capitis, and fungal skin infections. It is an analogue of naftifine. Terbinafine is 10-100 times more powerful in vitro than natifine. Terbinafine is extremely lipophilic, resulting in large concentrations in the stratum corneum, sebum, and

hair follicles, as well as effective binding, minimising the risk of reinfection. Terbinafine hydrochloride 250mg and 500mg tablets are commonly prescribed for oral consumption. Terbinafine is generally well tolerated when used orally or topically. Terbinafine cream and topical solution 1% have been proven to be effective in the treatment of tinea corporis, tinea cruris, tinea pedis, and cutaneous candidiasis, with mycological cure rates ranging from 69 to 100 percent after four weeks of treatment (depending on the severity of the infection).

- **Absorption**

Terbinafine is extremely lipophilic, resulting in high concentrations in the stratum corneum, sebum, and hair follicles, as well as efficient binding to them, minimising the risk of reinfection. For the major dermatophytes, pharmacokinetic studies revealed residual concentrations substantially above the MICs 7 days after topical administration. Terbinafine is an allyl amine derivative that is 10 to 100 times more powerful in vitro than naftifine.

- **Mechanism of action**

Terbinafine has a broad antifungal spectrum and inhibits the capacity of squalene epoxidase to catalyse squalene to ergosterol conversion. Cell death occurs when the manufacture of ergosterol, a sterol important for cellular integrity, is suppressed, and intracellular squalene accumulates. Terbinafine suppresses ergosterol production earlier than azole antifungals, without altering steroidogenesis related to cytochrome P-450. Its fungicidal rather than fungistatic activity may be due to this earlier method of action.

RELATED STUDIES

Neha Vij and R. Saudagar (2020) [1]: The pharmaceutical active must be kept at the treatment location for an effective duration of time in order to treat disorders of body tissues locally. Sweat, clothing, motions, and the ease with which they are washed away on contact with water are just a few of the issues that have limited the effectiveness and residence time of traditional topical formulations for treating fungal infections of the skin. This demands a longer period of treatment. As a result, a composition that clings to the infected skin surface and delivers an antifungal drug locally is required. Methods: The goal of this study is to develop a TH dosage form known as a 'film-forming gel,' which produces a thin, transparent film on the skin's surface when applied. Eudragit RS PO and hydroxypropyl cellulose were combined to create a matrix film that would allow the antifungal agent to be released for an extended period of time. 3 2 full factorial design was used to create the formulations. Drying time, drug release, antifungal activity, skin irritation, and stability investigations were all performed on them.

The pH, viscosity, drug content, effective dose volume, and mechanical properties of the film created after application were all measured, as well as bioadhesion and water vapour permeability. For various testing, all of the formulations produced results that were within acceptable ranges. The improved formulation has a 99.84 percent drug release rate and a 99.44 percent antifungal effectiveness rate. Conclusion: Such a formulation might be claimed to shorten the period of therapy, increase patient acceptance, and represent a breakthrough in the treatment of skin fungal diseases.

Sharma, Shivam& Vivek (2020) [2]: The goal of this work was to create and test a phytosome of terbinafine HCL in vitro in order to improve oral bioavailability. Using the solvent evaporation approach, a new phytosome of terbinafine hydrochloride (TFH) was created with a molar ratio (1:2) of drug and phospholipid. Particle size analyzer (PSA), % yield, microscopy, drug content, and transmission electron microscopy were used to determine the TFH-PC (TEM). Fourier transforms infrared spectroscopy was used to confirm that terbinafine HCL had made substantial contact with phospholipids (FTIR). The percentage entrapment efficiency of the formulation was determined to be between 76 and 90 percent in all relevant TFH-PC results. Using the dialysis membrane approach, roughly 65 percent to 79 percent of the drug was released from the TFH-PC formulation in vitro. As a result, Formulation (F3) was developed to ensure that phytosomes have superior physical properties and compatibility with drugs and phospholipids, making it easier to overcome the drug's ability to pass through the lipid-rich bio-membrane. Conclusion: A terbinafine-loaded phytosome was developed in this study to improve the oral bioavailability of a certain drug. As a result, the TER-HCL phytosome efficiently increased drug absorption in the form of phospholipids complex.

Amer, RehamI et al., (2020) [3]: Terbinafine hydrochloride (THCl) is an antifungal agent with a broad spectrum of activity. THCl has a 40% oral bioavailability, which increases the drug's dose frequency and, as a result, causes some systemic side effects. To distribute the drug topically, a sustained release THClnanosponges hydrogel was created. The researchers used pure THCl (drug), polyvinyl alcohol (emulsifier), and ethyl cellulose (EC, a polymer used to make nanosponges). The emulsion solvent evaporation process was used to successfully generate THClnanosponges. Different THCl:EC ratios and stirring rates were employed as independent variables in a 32 complete factorial design. Topical hydrogel was created using the optimum formula based on particle size and entrapment efficiency percent (EE). Except for F7 and F9, all formulations were identified in the nanosize range. EE percentages ranged from 33.05 to 90.10 percent. After 8 hours, THClnanosponges hydrogel released more than 90% of the drug and had the best in vivo skin deposition and antifungal efficacy. Higher stirring rates resulted

in finer emulsion globules and a considerable reduction in EE, whereas increasing the drug:EC ratio increased EE and particle size. When the drug was incorporated in entrapped form as nanosponges rather than unentrapped form, the drug release profile was delayed. THCl release was sustained for 8 hours using the nanosponges hydrogel. It had the most antifungal activity as well as the most skin deposition. THClnanosponges hydrogel is an improved therapeutic method for treating fungal infections on the skin.

VedavathiThavva and Srinivasa Rao Baratam (2019) [4]: The goal of this study was to develop and test Terbinafine hydrochloride microsponges using a quasi-emulsion solvent diffusion technology and a microsponge gel containing carbopol for controlled drug release while avoiding side effects. With six distinct drugs: polymer ratios, microsponges containing Terbinafine hydrochloride were successfully generated. Particle size, physical characterization, and in vitro release were all investigated in the formulations. A selected THCI microsponge (MS IV) was incorporated in different concentrations of carbopol and formulated as gels and evaluated for pH, viscosity, spreadability, drug content, in vitro release, antifungal activity, and in vivo studies due to its better results when compared to other microsponge formulations. THMG II outperformed the other three microsponge gel formulations with a pH of 6.2, viscosity of 3960 cps, spreadability of 18.1 g cm/s, drug content of 87.6%, and fickian drug release. Antifungal experiments revealed a zone of inhibition of 15.8 mm compared to 19.2 mm for the pure drug and 16.0 mm for the marketed formulation, as well as superior antifungal action on fungal induced guinea pig skin compared to control. Conclusion: The controlled release of terbinafine hydrochloride from the microsponge gel reduced adverse effects and significantly reduced the need of the gel for fungal treatment in this trial.

Celebi et al., (2014) [5]: The goal of this study was to create hydrogels and microemulsion (ME)-based gel formulations containing 1 percent terbinafine hydrochloride (TER-HCL), as well as to assess their efficacy in treating fungal infections. Chitosan, Carbopol® 974, and Natrosol® 250 polymers were used to make three distinct hydrogel formulations. A pseudo-ternary phase diagram was created, and a ME gel form containing 1% Carbopol 974 was created from the ME formulation. The characteristics of the prepared hyrogels were also investigated. After three months of storage at various temperatures, the physical stability of hydrogels and ME-based gels was assessed. A conventional dialysis membrane in phosphate buffer (pH 5.2) at 32 °C was used to remove TER-HCL from the gels and the commercial product (Lamisil®). The Natrosol gel released the most drug, followed by Carbopol gel, chitosan gel, commercial product, and microoemulsion-based gel in that order, according to the results of the in vitro

release research. All of the produced and marketed medicines were effective against Candida parapsilosis, Penicillium, Aspergillus niger, and Microsporum when tested in vitro for antifungal activity. These findings suggest that the Natrosol®-based hydrogel is a promising choice for TER-HCL topical administration.

Rompicherla et al., (2013) [6]: The goal of this study was to see how reduced vesicular size affected the characteristics of ethosomes when compared to the regular vesicular size of ethosomes as a topical drug delivery vehicle for Terbinafine hydrochloride (TH), an antifungal drug, in order to achieve optimal localised drug concentration and reduced dose frequency. Because oral administration of TH is prohibited due to severe side effects, topical treatment is advised. The residual time of commercially marketed TH creams, lotions, and sprays is relatively short at the target spot. Drug entrapment in vesicles improves drug localisation, solubility, and availability at the location, resulting in a dose decrease. Higher concentrations of alcohol in the form of hydroalcoholic or hydroglycolic phospholipid were used to make drug-containing ethosomes. Shape, particle size, and entrapment efficacy of sonicated and unsonicatedethosomes were examined. The use of an electronic microscope revealed not only important evidence for the presence of phospholipid vesicles in TH ethosomal systems, but also that sonicated ethosomes were more homogeneous in size and shape than unsonicatedethosomes. Ex vivo skin permeation, ex vivo drug release, and entrapment efficiency investigations were also conducted as part of the comparative inquiry. The release of the drug was governed by zero order release rate kinetics. The sonicated ethosomal formulation deposited more than 19.01 percent of the drug into the skin, compared to 2.57 percent for the unsonicatedethosomal formulation, according to a drug accumulation study. During stability tests, both sonicated and unsonicatedethosomes were found to be stable at refrigeration and room temperature. In sonicated ethosomes, drug accumulation in deep skin layers was shown to be comparatively higher, indicating increased localised drug and, as a result, lower dose frequency.

Debnath, Subhashis et al., (2012) [7]: Terbinafine hydrochloride is an antifungal drug that is synthesised. It is slightly soluble in water (3 mg/ml) and has a high stomach permeability. As a result, oral administration has a low bioavailability. To increase the bioavailability of terbinafine HCl, a nanoemulsion containing it was created. The aqueous titration method was used to create the pseudo-ternary phase diagrams. Different volume ratios of surfactant (Tween 80) and co-surfactant (Ethanol) were mixed (Smix) (1:0, 1:1, 1:2, 1:3, 1:4, 2:1, 3:1, 4:1). Based on the solubility study, olive oil was optimised as an oil phase. Oil (olive oil) and specific smix ratios were thoroughly mixed in different

volume ratios ranging from 1:7 to 7:1 for each phase diagram. For the study, different ratios of oil and smix (1:1, 1:2, 1:3, 1:4, 1:5, 1:6, 1:7, 2:1, 3:1, 4:1, 5:16:1, 7:1) were used to precisely delineate the phases' boundaries in phase diagrams. The drug release, dispersibility, viscosity, surfactant content, electroconductivity, and TEM analysis of the formed nanoemulsions were all assessed. When Terbinafine HCl was delivered as a nanoemulsion, in vivo experiments demonstrated a 2.38-fold improvement in bioavailability when compared to drug suspension.

Raja Kumar et al., (2012) [8]: In this study, transdermal patches of Terbinafine HCl were made with different concentrations of polymers such as HPMC, SCMC, and carbopol 934. These transdermal patches will be evaluated for physicochemical properties such as patch thickness uniformity ranging from 0.211 ± 0.016 mm to 0.232 ±0.013 mm, patch weight uniformity ranging from 0.312 ± 0.033 mg to 0.398 ± 0.021 mg, patch tensile strength ranging from 3.21± 0.114 to 4.62± 0.111 kg/mm^2, patch folding endurance ranging from 74.11 ± 4.231 to 97.56±6.231, drug content uniformity, and To determine the incompatibility, researchers used FTIR (Fourier Transform infrared) and DSC (differential scanning calorimetry).

MATERIALS AND METHODS:

Terbinafine hydrochloride, microcrystalline cellulose, hydroxyl propyl methyl cellulose, sodium starch glycolate, magnesium stearate, colloidal silicon dioxide.

Physical and chemical:

Characterization of Innovator: Formulation:

The innovator formulation (Tablets 250mg) was tested chemically and physically to characterize it to aid formulation development.

Comparative Dissolution Profile:

Comparative dissolution profile of Innovator Tablets 250 mg was studied in four different media - 0.1 N Hydrochloric acids, Phosphate buffer pH 6.8, and Acetate buffer pH 4.5and Citrate buffer pH 3.0.

Product: Innovator Tablets 250mg

Apparatus: USP TYPE II Paddle

Speed: 50rpm

Sampling Time: 10, 20, 30, 45, and until at least 95% of label content dissolved

Table 2 compares the dissolving profiles of four distinct media. Formulation of instant release tablets with various excipients:

Formulation of immediate release tablets by using different excipients:

The exploratory research, innovative product physical and chemical characterisation, and drug excipient compatibility study laid the groundwork for producing 300mg instant release tablets. The studies started with direct compression and subsequently moved on to wet granulation. The entire batch processing was carried out in a controlled environment. At a relative humidity of 40-50 percent RH and a temperature of 21-25 degrees Celsius, Physical criteria like loss on drying, average weight, disintegration time, hardness, and others, as well as chemical parameters like assay, dissolution, and related compounds, were assessed for the blend and tablets.

Process: -

- Terbinafine Hydrochloride, Microcrystalline Cellulose, and Sodium Starch Glycolate were weighed and sieved individually using #40 sieves. For ten minutes, all of the components were combined in a polybag.
- To make the binder solution, dissolve HPMC E-LV and HPLC E-MV inenough water to make a clear solution while stirring (For the different trial batches different binder solution was added respectively as mentioned in the table)
- Granulation- In this phase, the step-1 blend was granulated with the step-2 binder solution, and water was added to obtain wet mass.
- Step 3: The wet material was dried in the FBD for 40 minutes at 70°C and the LOD was evaluated (10 minutes at 90°C). LOD was tested after passing through #20 sieve.
- Colloidal silicon dioxide was sieved at #60 and sodium starch glycolate was sieved at #40 before being combined with step-4 granules in a polybag for 5 minutes.
- Magnesium Stearate was sieved through a #60 sieve and combined for 2 minutes in a polybag in step 5.
- Step-6 lubricating granules were used to compress the tablets. It was compacted into tablets with an 11.1mm biconcave punch with a break line on one side and plain on the other.

Experimental Design:

Table1: Formula for various trial batches with different binder solution and extragranular agents

S. No.	Ingredients	Trial batch no 1	Trial batch no 2	Trial batch no 3	Trial batch no 4	Trial batch no 5	Trial batch no 6	Trial batch no 7
		Quantity /tab mg	Quantity /tab mg	Quantity /tab mg	Quantity /tab mg	Quantity /tab mg	Quantity /tab mg	Quantity /tab mg
1	Terbinafine hydrochloride	281.3	281.3	281.3	281.3	281.3	281.3	281.3
2	Microcrystalline cellulose	60.5	82.7	80.7	60.7	73.2	60.7	74.2
3	Sodium starch glycolate	18	10	10	18	10	18	10
4	Colloidal silicon dioxide	4	-	4	4	4	4	-
	Binder solution							
5	HPMC E-MV	8	6	12	4	17.5	12	-
6	HPMC E-LV	12	-	-	6	-	8	17.5
7	Purified water	qs	100 ml	140 ml	qs	qs	qs	qs
	Extra granular							
8	Sodium starch glycolate	10	8	8	10	8	10	8
9	Magnesium	4	3	4	4	6	4	6

	stearate							
10	Colloidal silicon dioxide	2	3	2	2	-	2	3

Evaluation of immediate-release tablets:

The prepared batches' blends and tablets were assessed for compliance with official and unofficial in-process parameters.

Physical evaluation:

Loss on drying:

It is a wet-weight representation of moisture content that is determined as follows:

$\% LOD = W/W_t \times 100$

Where, W = Weight of water in sample

W_t = Total wt. of wet sample

IR balance at 105°C was used to calculate the LOD of unlubricated and lubricated blend samples.

Bulk density:

Bulk density is defined as the mass of a powder divided by the volume of the bulk.

In a 100ml graduated cylinder, a blend sample (20gm) was inserted. On a graduated cylinder, the volume of the material was recorded. The bulk density in gm/cm3 was estimated using the formula below.

Bulk density ($\rho 0$) = M/V_o

Where,

M = Mass of the powder; vo = Volume of the powder

Tapped density:

The ratio of the mass of the powder to the volume occupied by the powder after it has been tapped for a set period of time is known as the tapped density of the powder.

The blend sample under test was screened through sieve no. 18 and put into a 100 ml graduated cylinder with a weight of 20 grammes. The cylinder was tapped 500 times using the Bulk Density Apparatus, and the tapped volume V_f was recorded.

The formula was used to compute the tapped density in gm/cm3;

Tapped density (ρt) = M/Vf

Where,

M = Weight of sample powder taken

V_f = Tapped volume

Compressibility index:

The compressibility index is a measurement of the powder's ability to consolidate.

The compressibility index was computed using the formula after measuring the bulk and tapped densities.

C.I. = {(ρt-ρo)/ ρt} ×100

Where,

ρt = Tapped density

ρ0 = Bulk density

Hausner ratio:

The hausner ratio was estimated using the formula by measuring the tapped density and bulk density,

Hausner ratio = ρt/ρo

Where,

ρt = Tapped density

ρo = Bulk density

Angle of repose of final blend:

This is the angle θ as defined by the equation below;

$\tan \theta = h/d$

Where,

h = Powder bed height

d = Powder bed diameter

The repose graph was used to determine the angle of repose of the final blend.

Thickness:

Thickness: For all batches, thickness was measured in millimetres.

Hardness:

The tablets' hardness was determined using a schleuniger hardness tester. Five tablets were evaluated for each batch. For each batch of tablets, the hardness was measured in newtons (N).

Disintegration time:

Disintegration time refers to the process of breaking down a tablet into smaller particles or granules. Disintegration test apparatus was used to assess the disintegration time of the tablets. Six tablets were placed in each cylinder of the equipment, and tests were performed and disintegration times recorded. For each batch of tablets, the disintegration time was measured in minutes and seconds.

Friability:

Twenty tablets were weighed and placed in an Electrolabfriabilator, which was rotated at 25 rpm for four minutes. The tablets were dedusted and weighed afresh after each revolution. The formula was used to calculate the percentage of friability,

$\% F = \{1- (W_o/W)\} \times 100$

Where,

% F = Friability in percentage

W_o = Initial weight of tablet

W = Weight of tablets after revolution

Weight variation:

Twenty tablets were chosen at random from each batch and weighed individually. The weight of 20 tablets was determined as an average. If no more than two of the individual tablet weights differ from the average weight by more than the percentage stated, and none deviate by more than twice the percentage shown, the batch passes the weight variation test.

Assay (% of label claim):

Tablets from each batch were examined for assay (percentage of label claim) (percent of label claim). Each trial displays the batches' tests (percentage of label claim). In each trial, the plot of the comparative assay of distinct batches is displayed.

In-vitro release profile study:

Using a USP type II dissolution apparatus, an in-vitro release profile study of an immediate release tablet was conducted. At the start of each test, the tablet was retained and rotated at 50rpm. The release rate investigation employed 500ml of water as the medium. Throughout the investigation, the whole assembly was kept at 37 ± 0.5 °C, and a 10ml sample was taken at intervals of 10, 20, 30, 45 minutes, or until 95 percent of the active substance was dissolved.

CDER dissolving technique:

The CDER dissolution method was carried out using the following parameters: Type II (basket) speed 30rpm, medium 3.0 citrate buffer volume 500mL, and sample times of 10, 20, 30, 45 minutes, or until at least 95% of the label content was dissolved. Individual trials reveal the findings of in-vitro release profile (Dissolution profile) studies of batches. In each trial, a plot of the comparative dissolution profile of distinct batches is displayed.

RESULTS AND DISCUSSION:

The preliminary studies of the drug substance (Active) met the quality requirements. Drying loss of 0.08 percent w/w was recorded. Any individual unknown contaminant and total impurity not discovered are related substances. On a dried basis, the drug was assayed and 99.9% w/w was obtained.

Characterization of the innovative formulation in terms of its physical and chemical properties:

The diameter of the innovative formulation is 11.22mm, the weight of the tablets is 404.3 mg, and the hardness is 71-95N, according to physical characterization.

The chemical characterization of the innovative formulation revealed a 100% assay, the highest unknown impurity of 0.10 percent w/w, total known impurity of 0.30% w/w, and total impurity of 0.40 percent w/w.

Table 2: Comparative Dissolution Profile of in four different media of innovator formulation

Brand Name	**Innovator Tablets DASKIL TABLETS 250mg**			
B. No.	**0316**			
Medium	**0.1 N HCL**	**pH 4.5 Acidic buffer**	**pH 6.8 Phosphate buffer**	**pH 3.0 Citrate buffer**
Time (min)	**%Release**	**%Release**	**% Release**	**%Release**
0	0	0	0	0
5	18	27	0.0	0.0
10	50.3	34.7	0.0	79.2
20	68.7	39	0.0	91.5
30	79.7	42.8	0.0	94.7
45	86.5	44	0.0	95.3

In 0.1N hydrochloric acid, the dissolving profile of Innovator Daskil Tablets 250 mg revealed sluggish drug release. The dissolving profile in an acidic buffer pH 4.5 revealed that the drug was released slowly. In phosphate buffer pH 6.8, the dissolution profile revealed no drug release. In comparison to all other pH 3.0 citrate buffers, the pH 3.0 citrate buffer showed 79-95 percent drug release in 45 minute.

Table 3: Results of the Physical Evaluation

Batch No.	TRL/01	TRL/02	TRL/03	TRL/04	TRL/05	TRL/06	TRL/07
Weight per tablet (mg)	399	406	402	407	413	402	413
In process Parameters	Uncoated	Uncoated	Uncoated	Uncoated	Uncoated	Uncoated	Uncoated
LOD	1.75%	3.0%	1.8%	1.75%	2.13%	1.8%	2.7%
Bulk Density (g/ml)	0.39	0.37	0.42	0.39	0.413	0.39	0.403
Tapped Density (g/ml)	0.51	0.52	0.55	0.51	0.511	0.5	0.525
Carr Index	23.5	28.4	23.63	23.5	19.6	22	23.23
Hausner Ratio	1.30	1.40	1.30	1.30	1.24	1.28	1.30
% fine Passed Through 60 Mesh	44	39	24	41	28	32	34
Angle of repose of final blend	27	23	23	23.9	26.56	29	30.4

Thickness (mm)	4.89-4.93	4.48-4.5	4.48-4.5	4.92-4.98	4.77-4.8	4.93-4.98	4.7-4.8
Hardness (N)	110-122	193-206	193-206	110-128	120-121	115-138	95-115
Disintegration Time (min.sec)	5min50 sec 5min55 sec	13min40 sec 14min15 sec	15min50 sec 16min45 sec	5min50 sec 6min45 sec	8min15sec 9min50sec	1min25sec 1min30sec	1min11 sec 1min5sec
Friability (%) (100 rotation)	0.09%	0.09 %	0.09 %	0.09 %	0.19%	0.11 %	0.12%

Table 4: In-vitro release profile (dissolution profile) of batches

Brand Name	**Terbinafine hydrochloride Tablet 250 mg**						
	% Drug Release (pH 3.0 Citrate buffer)						
Time (min)	TRL/01	TRL/02	TRL/03	TRL/04	TRL/05	TRL/06	TRL/07
10	56	69	56	89	90	92	96
20	69	75	89	95	96	94	97
30	77	76	97	96	95	95	98
45	89	87	99	97	94	96	99

Table 5: Comparative invitro release profile of formulation with innovator formulation.

Brand	**Terbinafine hydrochlorid**	**Innovat**	**Terbinafine hydrochlori**	**Innovat**	**Terbinafine hydrochlori**	**Innovat**	**Terbinafine hydrochlori**	**Innovat**

name	e 250mg	or DASKIL tablet 250mg	de 250mg	or DASKIL tablet 250mg	de 250mg	or DASKIL tablet 250mg	de 250mg	or DASKIL tablet 250mg
Batch no	TRL/07	DAS 123	TRL/07	DAS 123	TRL/07	DAS 123	TRL/07	DAS 123
Medium	0.1N HCL	0.1N HCL	PH 6.8 buffer	PH 6.8 buffer	PH 4.5 buffer	PH 4.5 buffer	PH 3.0 Citrate buffer	PH 3.0 Citrate buffer
Time (min)	%Release	%Release	%Release	%Release	%Release	%Release	%Release	%Release
10	48	50.3	0	0	32.6	34.7	96	79.2
20	65	68.7	0	0	38	39	97	91.5
30	80	79.7	0	0	41	42.8	98	94.7
45	87	86.5	0	0	43	44	99	95.3

For the trial batches 6 and 7, an accelerated stability investigation was carried out over a 90-day period. It has a 99.8% and 99.8% assay, respectively. The innovative formulation had a thickness of 4.5-4.9mm, a weight of 404.3mg, and a hardness of 71-95N, according to physical characterization. The assay of 102 percent was found in the chemical analysis of the innovative formulation. The release of drug is greater in the 3.0 citrate buffer. The average weight, disintegration time, and hardness of formulation batch nos. 7 and 6 were all stable at 400°C, ±20°C, 75 percent RH, and ±5% relative humidity. Batches were monitored for a three-month period. Individual maximum impurity increased from 0.30 to 0.35 percent, while total impurity climbed from 0.40 to 0.47 percent. The dissolution of batch no. 7 is comparable to that of the innovator 0.1N HCL dissolving medium. Batch no.07 exhibits 100.4 percent drug release at 45

minutes, whereas innovator shows 102 percent drug release. In dissolution medium of 0.1N HCl, pH 6.8, pH 4.5, and pH 3.0 citrate buffer at USP type II paddle, batch no:07 exhibits a same percentage of drug release as the innovator.

CONCLUSION:

The purpose of the preformulation research was to ensure that the medicine and the excipient were compatible. Some of the excipients were chosen for formulation development based on the results of the preformulation study. Using different excipients in varying quantities and combinations by wet granulation technology, several formulations were devised to match the parameter with the marketed product. With the final formula, the formulation development was accomplished. According to ICH and FDA requirements, a stability study was undertaken on batch 06 and batch 07 tablets. After one month, the tablets were tested for in vitro dissolving and in vitro release profile. During the study period, no significant changes in any of the examined parameters were identified, indicating that the formulation was stable. The stability study demonstrated that the dissolution profile had not changed significantly. Based on the findings of all formulations, it was determined that the produced formulation of an immediate release tablet containing terbinafine hydrochloride medication was identical to the marketed product in every way and was resistant to temperature and humidity effects.

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