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Formulation and design of finasteride coated microneedles

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ABSTRACT

The elaborated reviews of prepared coated microneedles and their breadth of relevancy are inadequate. Cooperate with a category of medicines referred to as 5-alpha reductase inhibitors. Finasteride good things temperate prostatic hyperplasia by way of blocking the overall body's steel production going from a male hormone for which causes the overall prostate to particularize. Everything good things alopecia by way of blocking the body's production of a male hormone inside the scalp that prevents hair growth. A proportion going from alcohol found in marketed formulation the as permeation vertical stabiliser was famous to damaged hair, follicle as well as scalp epidermal polymers dehydration. The finishing line of the overall written report was once to approve the overall permeation of medicine with the aid of microneedles, thus lowering the general concentration and wear away scalp cells. Under a motic microscope, the length of uncoated microneedle and coated microneedle was found to be 634.6μ and 696.9μ precisely which either confirmed the coat over the microneedle. The percentage drug content of f6 formulation was shown at 98.80 $\pm$ 1.60 %. It encounters therefore the percentage going from drug discharge delight in coated microneedles and the marketed formulation was 96.82% and 93.93% individually. The f6 microneedle formulation encounter as far as to check zero-order release kinetics R^2 value 0.737. Spectacular drug discharge analytic thinking of soaked microneedles encounter ultimate come close with the marketed solution of minoxidil of the same strength. Accelerated stability study of 30 days at accelerated temperature stipulations confirmed an insignificant speed of deterioration.

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INTRODUCTION

Microneedles are a loan-blend between canisters and transdermal patches. Then we are usually some micron in width as well as mountain range delight in 1-100 microns successful length. It is slighter than a hypodermic needle; it hurts too little it penetrated the outside and throw up several advantages in comparison to plain needle technologies [1].

Microneedles can stick invented to be long-run fully permeate the overall stratum corneum, excluding short enough not to venipuncture nerve endings. The current equalizes the probabilities going from pain. Virus infection. It appears therefore the flux of small molecules take pleasure in diclofenac, methyl nicotinate, in addition to calcein was once magnified by microneedle interfaces [2].

In addition, microneedles have been inspected to enhance the overall flux of diffusion as large proteins like fluorescein isothiocyanate-labelled dextran, insulin, bovine serum albumin, plasmid DNA,

and nanospheres. Microneedles might work micro furnaces large as far as delivering drug loaded liposomes into the skin [3].

A variety of materials used for the preparation of microneedles are silicon, metal, and polymers. Type of molecules that can be delivered via microneedles is hydrophilic drugs, larger size drug polymers, and even small particulate carrier system. Alopecia is a very common problem seen both in men and women. A person suffering from hair loss hesitates to present himself in public [4].

Till now, in India minoxidil is optimized as a topical solution in a binary compound military vehicle inside the treatment of alopecia which bestows application in place for 4 hrs to be effective. Finasteride has a serum half-life of 4-5 weeks. The slow penetration of finasteride means that serum rarefaction of finasteride don't reach high therapeutic levels, significantly when applied to the frontal area, where the stratum corneum and entire epidermis is milder have high melanin content [5]. A high percentage of alcohol (90%) is employed as a penetration enhancer in the manufacturing of Finasteride formulations which causes dehydration of hair, hair follicle, and scalp epidermal cells. At this high concentration of ethanol, it causes the death of epidermal cells and prevents hair growth [6].

Hence to enhance the penetration of Finasteride and reduce the side effects of ethanol, Finasteride was coated on microneedles. Thus coated microneedles for the scalp can be used to increase the serum level of minoxidil without an increase in drug concentration. The most essential benefits of microneedles over handed over needles serves as, whenever it can be infused into mostly skin it does now not pass the general stratum corneum, which is the superficial 10-15 μm of the general skin [7].

MATERIALS & METHODS

Stainless steel microneedle was once purchased from Coherent medical system, New Delhi; Finasteride became purchased free of charge sample from Manish Pharmaceuticals, Bhosari, Eudragit E 100, Polyethylene glycol was a gift stratified sample of Bliss chemicals & pharmaceuticals India Ltd. (Thane). Ethanol was purchased from LOBA chemicals and other ingredients used were of Analytical grade.

Methodology

Fourier transforms infrared spectroscopy

The Finasteride turned into tape-recorded using Fourier transform infrared spectrophotometer. A clear pellet of your mixture used to be formed as well as settled in the overall stratified representative sample pin as well as scanned over an amplitude range of spectrum of 4000 – 400cm-1 [8].

Solubility study

The Finasteride was determined in organic solvents like propranolol, butanol, PEG and water. A redundant amount of Finasteride consider boot each vial that included 1ml going from solvent. The assortment used to be stirred up and sonicated that one may facilitate prudish mixing of the drug [9]. The mixture used to be agitated as 72 hrs at 40$\pm$0.5°C within a rotary orbital shaker. Further, the assortment turned into centrifuged at 3,000 revolutions per minute as 15 min, among filtration through Whatman filter paper.

Selection of polymer for coat formation

Hydroxyl propyl methylcellulose, ethylcellulose, sodium carboxymethylcellulose, carbopol, and eudragit E 100 were used to prepare coating solutions [10]. Respective concentrations of 1%, 2%, 3%, and 4 % of each polymer were prepared in a mixture of ethanol and Polyethylene glycol (3:2); the resulting solutions were examined for their coating ability.

Formulation and Development

Preparation of coating solution

The solution prepared from eudragit E 100 in ethanol. Polyethylene glycol was to boot the eudragit solution. To this 0.1 gm (2%) of the drug was added and therefore the mixture used to be stirred at 500 rpm on a homogenizer at 30 minutes. The resulting solution was used to coat the microneedles [11].

Coating of microneedles

The coating solutions of various concentrations of eudragit E 100 were prepared as described above. Employing a microsyringe the coating solution was deposited on each needle. To minimize coat formation on the surface of the roller, approximately half of the microneedles were coated and the roller was inverted and allowed to air dry for 10 minutes. Due to the tensile effect, the coating solution was preserved preferably on the microneedles. Then, the remaining needles were individually coated and allowed to air dry for 10 minutes in the inverted position. After a complete coating of all the microneedles, the roller was then allowed to dry in a hot air oven at 37^{o}C for 30 minutes [12]. The total coating solution consumed was calculated by the subtracting final weight of the coating solution from the initial weight after coating the microneedles. The composition of finasteride coated microneedles

Table 1: Composition of Finasteride coated microneedle

SI.No	Excipients	F1	F2	F3	F4	F5	F6
1	Finasteride (mg)	0.1	0.1	0.1	0.1	0.1	0.1
2	Eudragit E 100 (mg)	0.1	0.1	0.20	0.20	0.15	0.15
3	Polyethylene glycol (ml)	1	1	3	3	2	2
4	Ethanol (ml)	2	2	4	4	3	3
5	Total Volume in ml	5	5	5	5	5	5

Table 2: FTIR spectrum of Finasteride & Mixture of compounds

FTIR Spectrum	IR absorption bands (cm-1)		Bond	Functional group
	Observed peak	Characteristic peak		
Finasteride	3678.49	3000-3700	O-H strech	Alkenes, aromatic ring
	3616.39	3000-3700	O-H strech	Alkenes, aromatic ring
	2907.11	2500-3000	C-H strech	Alkenes, Aromatic ring
	2761.87	2500-3000	C-H strech	Alkenes, Aromatic ring
	2360.72	2100.2660	C=C strech	alkynes
	1707.13	1600-1900	C=O strech	Aldehyde, ketones.
Eudragit E 100	3623.09	3000-3700	O-H strech	Alkenes,aromatic
	3448.80	3000-3700	O-Hstrech	Alkenes,aromatic
	2700.81	2500-3000	C-H stretch	Alkenes, Aromatic ring
	2598.57	2500-3000	C-H stretch	Alkenes, Aromatic ring
	2212.79	2100-2660	C=Cstrech	alkynes
Mixture	3682.31	3000-3700	O-Hstrech	Alkenes, aromatic
	3447.12	3000-3700	O-Hstrech	Alkenes, aromatic
	2718.03	2500-3000	C-Hstrech	Alkenes, aromatic ring
	2144.86	2100-2660	C=Cstrech	Alkynes

Table 3: Observations of solubility study in the selected solvent

Solvent	Solubility (mg/ml)
Methanol	0.232
Ethanol	0.100
Butanol	0.070
Water	0.011

Table 4: Valuation of Coated Microneedle Formulations

Formulation	Appearance	Drug content (%)± S.D.
F1	Uniform	95.20 ± 1.83
F2	Uniform	92.50 ± 2.53
F3	Uniform	94.70 ± 1.53
F4	Uniform	84.94 ± 1.63
F5	Uniform	91.34 ± 1.56
F6	Uniform	98.80 ± 1.60

Table 5: In- Vitro studies drug release Finasteride coated microneedles

Time (Mints)	% Drug Release					
	F1	F2	F3	F4	F5	F6
10	16.86	15.28	13.21	11.06	10.17	13.89
20	25.98	28.98	22.75	25.76	20.12	24.25
40	33.16	35.36	35.34	34.56	39.15	33.67
60	42.18	41.46	48.25	46.24	44.21	42.86
70	52.86	51.93	53.53	56.22	65.32	51.66
80	72.56	69.50	68.32	68.90	75.42	60.88
90	84.46	80.34	73.45	89.34	85.35	81.45
100	91.04	90.73	89.54	92.71	93.13	96.82

Table 6: Drug release kinetics Finasteride coated microneedles

Order of Process		Formulation code					
		F1	F2	F3	F4	F5	F6
Zero-order	R2	0.961	0.967	0.963	0.968	0.921	0.967
First-order	R2	0.974	0.979	0.975	0.973	0.965	0.961
Higuchi	R2	0.984	0.981	0.984	0.987	0.986	0.983
Hixon	R2	0.853	0.880	0.980	0.927	0.879	0.922
Korsmeyer	R2	0.853	0.952	0.840	0.918	0.873	0.835
		0.758	0.755	0.835	0.758	0.792	0.737

Table 7: Cumulative percent drug release vs time of coated microneedles & marketed formulation

Time (Min)	% Drug Release	
	F6	Marketed Formulation
10	13.89	11.06
20	24.25	20.52
40	33.67	30.32
60	42.86	40.36
70	51.66	49.25
80	60.88	59.62
90	81.45	79.31
100	96.82	93.93

Table 8: Observations of accelerated stability study (F6 Formulation) (mean ± SD, n=3)

Time	Appearance	Drug content (%)
Initial (0 Day)	Uniform	98.90 ± 0.78
10 days	Uniform	98.40± 0.42
20 days	Uniform	97.83 ± 0.73
30 days	Uniform	97.52 ± 0.53

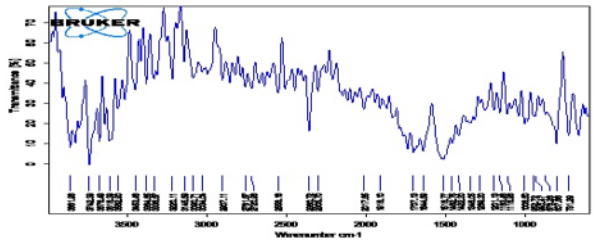

Figure 1: FTIR Spectra of Finasteride

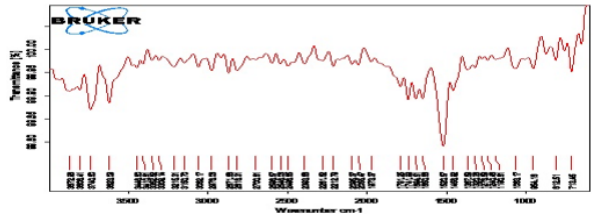

Figure 2: Spectra of Eudragit E100

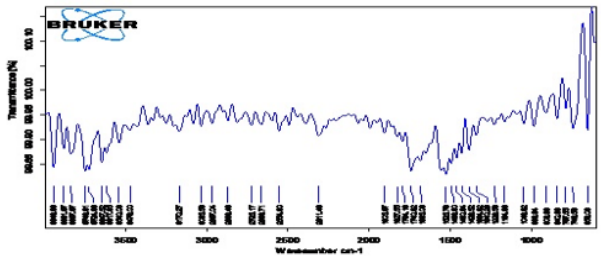

Figure 3: Spectra of Polyethylene glycol

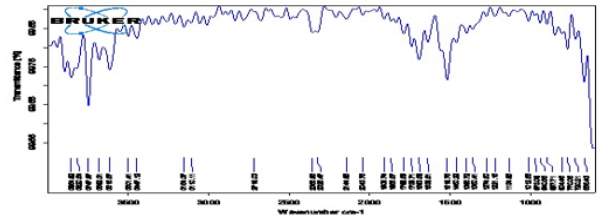

Figure 4: Spectra of Mixtures

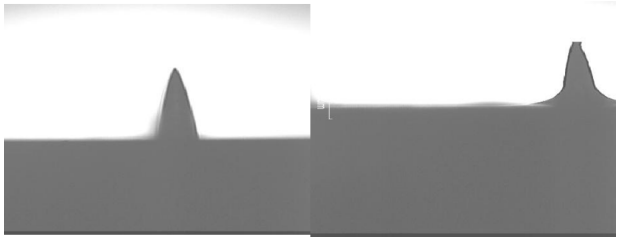

Figure 5: Motic image of a) plain microneedle and b) coated microneedle

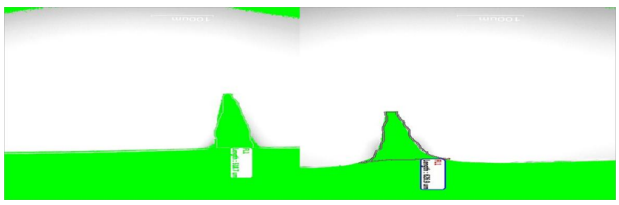

Figure 6: Length difference: a) plain microneedle and b) coated microneedle

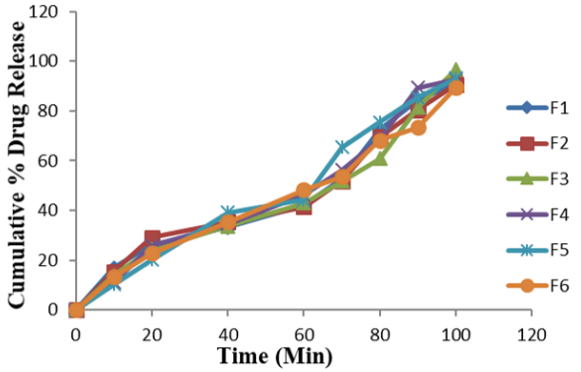

Figure 7: *In-Vitro* Drug Release Profile of Finasteride coated microneedles

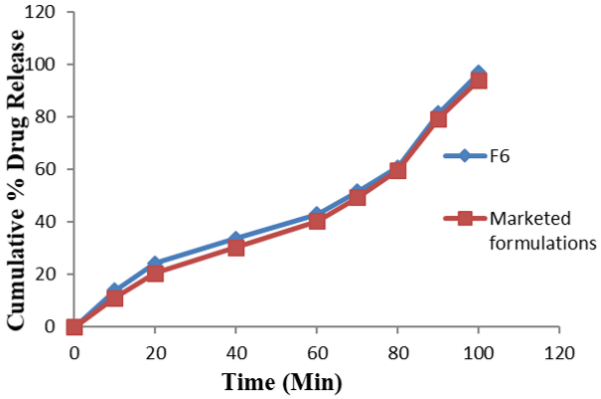

Figure 8: Graph of cumulative percent drug release vs time of coated microneedles and marketed formulation

as shown in Table 1.

Evaluation of Coated Microneedles

Measurement of coating dimension

The permanence of the coated microneedle was calculated and compared with the uncoated microneedle with the help of a motic microscope.

Percent Drug content

To determine the drug content entire roller of coated microneedles was soaked in 3 ml of phosphate buffer pH 7.4 in anticipation of them all the coat was once dissolved [13]. The UV Visible Spectrophotometry at λmax235 nm after appropriate dilutions.

In-vitro drug release study

The coated microneedles convey out in Keshary–Chien diffusion cell using a cellophane membrane. The receptor compartment was once packed with 100 ml of phosphate buffer in pH 7.4. A coated microneedle roller was rolled once on the cellophane membrane. The donor compartment was then placed on the membrane. The temperature used to be maintained 37±0.5^{o}C. An aliquot of 1 ml was withdrawn at a preset time interval from the

receptor compartment as well as substituted with 1 ml of phosphate buffer pH 7.4. The drug put concentration on the receptor fluid was determined by UV spectrophotometer at 235 nm. Marketed Finasteride solution (1 ml) was applied to the cellophane membrane. The treated membrane was similarly mounted on the Kesharychien diffusion cell as described above. An aliquot of 1 ml was withdrawn at preset intervals of time [14]. The concentration was determined by UV Spectrophotometry at 235 nm after appropriate dilutions. Drug release profiles of coated microneedles and marketed preparation were compared.

Accelerated stability studies

The coated microneedles stored in plastic casings were placed in a multiple stability chamber maintained at $400^oC \pm 20^oC$, $75 \pm 5\%$ RH for 30 days. The coated microneedles were withdrawn at 0, 10, 20, and 30 days [5]. Drug content and microneedle tectonics of coated microneedles were evaluated at each time interval.

RESULTS AND DISCUSSION

Drug Polymer Compatibility study

FTIR Spectroscopy

The IR spectrum of a somatogenic mixture of Finasteride and eudragit E 100 was recorded on Jasco FTIR-1100 spectrophotometer by the KBr disk method as shown in Figures 1, 2, 3 and 4. The result showed the presence of all characteristic peaks compared with standard peaks. The no deviation within the spectrum of your drug was observed. The current indicated no strong interaction between the drug and the polymer as shown in Table 2.

Solubility studies

It was exonerated from the solubility studies that the solubility of Finasteride in water was the least amongst the selected solvents; whereas it was found maximum in Polyethylene glycol. Also, it was observed that the solubility of Finasteride was inversely proportional to the carbon chain length of the monohydric alcoholic solvents considered for the study. The highest solubility of Finasteride in Polyethylene glycol was observed which may produce the overall presence of 2 hydroxyl groups in the solvent. Also, Polyethylene glycol was used as a moisturizing agent in many topical formulations. Hence it was chosen to elevate lyophilization of dermal cells caused due to ethanol as shown in Table 3.

Selection of polymer

From the various coating solutions prepared, all the polymers failed to coat microneedles except eudragit E 100. There was no coat formation observed on the microneedles when coated with hydroxyl propyl methylcellulose, ethylcellulose, carbopol, and sodium carboxymethylcellulose. Hence eudragit E 100 was selected as a coat forming polymer. From the literature, it was found that eudragit E 100 showed maximum solubility in alcohol.

Formulation of coated microneedle

If the dip-coating method would have adopted for coating of microneedles, which was easier as compared to coat each needle, this would have resulted in the coating of roller surface in addition to microneedles. The amount coated on the roller surface would not have been effectively administered while actual application. Hence this would have resulted in an administrative portion of formulation in turn increased the cost of manufacturing. Therefore coating of each microneedle, inversion of roller for drying, and further coating were adopted for efficient formulation development the physical appearance of the coat after observation under motic microscope showed complete coat formation over the microneedle surface and less at the base.

Evaluation of coated microneedles

Motic image

As it was clear from as shown in Figure 5 that the plain microneedles showed sharp tips whereas coated microneedles showed blunt tips. This depicted the presence of a coat on microneedles. Under a motic microscope, the length of uncoated microneedle and coated microneedle was found to be 634.6 μ and 696.9 μ severally which further confirmed coat over the microneedle as shown in Figure 6.

Percent of drug content

All the formulations were comparable with each other as shown in Table 4.

In-vitro drug release

The drug release of Finasteride from coated microneedle formulations was also compared with the marketed formulation as shown in Table 7 and Figure 8. It was found therefore, the percent consisting of drug release from coated microneedles and the marketed formulation was 96.82 % and 93.93% respectively as shown in Table 5 & Figure 7. The F6 microneedle formulation comes across to observe zero-order release kinetics R^2 value 0.737 as exposed in Table 6.

Accelerated stability study

It was observed that the coated microneedle formulation showed no significant change in appear-

ance as well as drug content when the samples were kept at an accelerated condition of 40^{o}C $\pm$ 2^{o}C, 75 $\pm$ 5% RH for 30 days. The rate of degradation was calculated to be 0.036 mg/day at above mentioned accelerated condition. To predict the stability of the formulation, a study at an additional accelerated temperature and humidity was needed as shown in Table 8.

CONCLUSION

It was concluded that microneedle formulation showed comparable drug permeation while the concentration of ethanol, which was used as permeation enhancer in the marketed formulation was reduced the same was chosen for the study. In the drug and excipient compatibility studies, there is no variation within the spectrum going from the drug was observed. This represented the presence of a coat on microneedles. Under a motic microscope, the length of uncoated microneedle and coated microneedle was found to be 634.6 μ and 696.9 μ. The drug release of Finasteride from coated microneedle formulations was also compared with the marketed formulation. It was found therefore the percent going from drug discharge from coated microneedles and marketed product was 96.82% and 93.93% respectively. The F6 microneedle formulation was found to observe zero-order release kinetics R^2 value 0.737. The release order kinetics of mechanism Non-fickian process. It was observed that the coated microneedle formulation flaunted no deviation in appearance as well as drug content when the samples were kept at an accelerated condition of 40^{o}C $\pm$ 2^{o}C, 75 $\pm$ 5% RH for 30 days.

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Conflict of interest

The authors attest that they have no conflict in this study.

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