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Research Article

Investigation of transdermal patches of fenugreek seed extract for the treatment of diabetes mellitus

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ABSTRACT

The present study reports the Investigation of Transdermal patches of Fenugreek seed extract for the treatment of Diabetes mellitus. Fenugreek seed extract was obtained from the Fenugreek seed (Trigonella foenumgraecum) belongs to the family Leguminosae. Used in the treatment diabetes mellitus, lower blood cholesterol level etc. It contains active constituents like trigonelline, choline etc. which involved in producing the antidiabetic activities and it also contain galactomannans content of the extract was responsible for the skin hydration. Therefore, it is possible that a topical formulation of fenugreek extract could enhance permeation and absorbed mainly at a specific absorption site in the skin. Transdermal patches containing fenugreek extract was formulated and evaluated for various parameters. The drug content show drug release of almost 90% after 6hr. Out of different formulation 2:2 ratio was found to have highest release. The results demonstrate that the controlled release from a transdermal drug delivery system also enhance better therapeutic efficacy, improved patient compliance and side effect associated with conventional drugs can be avoided.

Key Words: Transdermal patch, Fenugreek seed extract, Trigonelline, Diabetes mellitus

INTRODUCTION

Transdermal drug delivery systems are adhesive drug devices of defined surface area that deliver a predetermined amount of drug to the surface of intact skin at a pre-programmed rate. These systems input the drug at appropriate rates to maintain suitable plasma drug levels for therapeutic efficacy [1]. Transdermal delivery of drug for systemic treatment of diseases has acquired increasing interest in recent years due to its potential in avoiding the hepatic first pass metabolism, thus achieving high systemic bioavailability of drugs which undergo either considerable or extensive first pass metabolism and they are capable of sustaining the drug release for prolonged period of time. Moreover, it provides suitability for self administration and rapid termination of drug needed, leading to better patient compliance [2]. Despite these advantages, only a limited number of drugs can be administered percutaneously, due to low skin permeability of most drugs. The stratum corneum was recognized as an excellent barrier against skin penetration. To overcome these problems, vehicles, penetration enhancers such as DMSO (Dimethyl sulfoxide), Pyrollidone, Urea will be used and electro transport facilitated transdermal systems have been

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attempted in the development of an effect if transdermal delivery of many drugs [3].

Basic principles of transdermal permeation includes, topically applied drug must penetrate the statumcorneum, the skin penetration barrier. Drug molecule may diffuse through the skin by three different routes intact statumcorneum, the hair follicle region, and the sweat glands [4]. In the initial transient diffusion stage, dry molecules may penetrate the skin along the hair follicles or sweat ducts and then be absorbed through the follicular epithelium and the sebaceous glands. When a steady state has been reached, diffusion through the statumcorneum becomes the dominant pathway.

Herbal therapy provides rational means for treatment of many internal diseases, which are considered to be obstinate and incurable in other system of medicine. It lays a great deal of emphasis upon the maintenance of positive health of an individual. Its main aim is to prevent and cure diseases. Herbal patches are medicated patches which are formulated now a day in large quantity for many medicines due to its advantages of less side effect and better compliance for patient while using it. With a resurgence of interest in herbals all over the world, India can become a major player in global market for herbal products [5].

Diabetes mellitus (DM) is the commonest endocrine disorder characterized by hyperglycaemia, glycosuria, hyperlipaemia, negative nitrogen balance. It leads to high blood glucose concentration and disturbance in carbohydrate, fat and protein metabolism. For its therapy, along with the synthetic drugs, many agents of the plant origin are also in use particularly for the treatment of noninsulin dependent diabetes mellitus (NIDDM)[6].

Fenugreek (Trigonella foenumgraecum) is one among the many herbs that have been studied for antidiabetic activity; fenugreek is an annual herb that belongs to the family Leguminosae. Used as food and for medicinal purposes. It is a good source of many essential elements such as iron, phosphorus and sulfur. Seeds can inhibit cancer of the liver, lower blood cholesterol levels and also have an anti-diabetic effect. The active constituents involved in producing the antidiabetic activities are pyridine type alkaloids like gentianine, trigonelline, choline, flavanoids-orientin, vitexin, quercetin; steroidal saponins –diosgenin, yamogenin, and gitogenin. It is also used in the treatment of late-onset diabetes, poor digestion (especially in convalescence), insufficient lactation, painful menstruation, labour pains etc. Fenugreek seed has been known to reduce glucose levels in type 2 diabetes and may also help to do so in type 1 (insulin-dependent) diabetes. It may increase plasma insulin level in vivo.[7] Its major free amino acid 4- hydroxyisoleucine stimulates insulin secretion from perfused pancreas *in vitro*. Moreover, the effect of topical application of fenugreek seed was studied and was reported that the galactomannans content of the extract was responsible for the skin hydration. The statumcorneum of the skin epidermis when hydrated is known to be permeable to many herb including drugs [8]. Therefore it is possible that a topical formulation of fenugreek extract could enhance permeation and absorption of the active constituents involved in producing the antidiabetic activities such as pyridine type alkaloids like gentianine, trigonelline, choline, flavanoids-orientin, vitexin, quercetin; steroidal saponins –diosgenin, yamogenin, and gitogenin through the skin and into the systemic circulation, more so if the extract is administered as a transdermal patch.[9] Therefore, in the present work attempt was made to formulate transdermal patches of fenugreek seed extract for controlled release of drug for reducing excess of diabetes mellitus.

MATERIALS AND METHODS:

Materials: Hydroxy propyl methyl cellulose (HPMC) E15-LV, Hydroxy propyl methyl cellulose (HPMC) 15CPS, Hydroxy propyl methyl cellulose (HPMC) 50CPS and Disodium methyl sulfoxide (DMSO) was purchased from Central drug house (p) LTD, New Delhi. Propylene glycol and Ethanol was purchased from Merk India Pvt. Ltd, Mumbai, India. All the chemicals/ reagents were used of analytical grade.

Formulation of Transdermal films of fenugreek seed extract: The transdermal films of fenugreek seed extract were prepared by Petri plate technique. [10, 11]

Preparation of casting solutions: The casting solutions was prepared by dissolving weighed quantities of polymers of different ratio in hydro alcoholic solution (Ethanol:Water) using a mechanical stirrer at 500 rpm for 2 h, then kept for swelling one day. The extract 2 g was dissolved in hydro alcoholic solution using a mechanical stirrer at 500 rpm for 3 h and added to the above polymer solution along with propylene glycol, as plasticizer, thoroughly mixed to form a homogeneous mixture using a mechanical stirrer at 500 rpm for 2 h. The volume was made up to 40 ml with distilled water. Entrapped air bubbles were removed by applying vacuum.

Preparation of Transdermal films: The casting solution (40 ml) was poured into petri-plates and dried at 60 ^{0}C temperature for 24 h in a hot air

oven. The films were removed by peeling and cut into square dimension of 3 cm x 3 cm (9 cm^2) such that each films contained 6.058 mg of Trigonelline. These films were kept in dessicator for further drying and wrapped in aluminium foil. To ensure one way flux of the drug during drug release studies backing layer was fabricated ethyl cellulose backing layer using cyano acrylate glue. Transdermal films were prepared with different polymer ratio, plasticizer concentration and permeation enhancers.

Evaluation of Transdermal films:

Visual Inspection*:* The prepared films were visually observed for color, transparency and homogeneity to assess some organoleptic properties.

Film Thickness*:* The thickness of the films was measured at five different places on a single patch of each formulation using a screw gauge and the mean values were calculated.[12]

Weight Variation: Films 2 × 3 cm2 in size were weighed on an electronic balance. The measurements were carried out in triplicates.[13]

Drug Content: One film from each formulation was cut in to small pieces was transferred into a 100 ml beaker containing about 50 ml of phosphate buffer using a mechanical stirrer at 500 rpm for 6 h and filtered and the volume was made to 100 ml with phosphate buffer (pH 7.2). Suitable dilutions were prepared with phosphate buffer (pH 7.2). The absorbance will be measured using UV spectrophotometer (V-630, JASCO, Japan) at λ max 263 nm.

Folding Endurance: This gives an indication of the brittleness of the film. The film was repeatedly folded in the same spot until it broke. The folding endurance was taken as a function of the number of times the film is folded before breakage. The experiment was done in triplicates and the mean ±SD was calculated.[14]

Tensile Strength: This mechanical property was evaluated using Tensile Strength Apparatus. The pressure gauge was selected depending on the sample to be tested by turning the gauge sector switch, Films of 3cm diameter free from air bubbles or physical imperfections were placed on the diaphragm plate and the wheel on top of the diaphragm place was rotated till it fits securely on the sample and does not rotate any further. The 'Push' button" was pressed till the sample bursts. The pressure gauge directly gives readings in Kg/cm^2. Measurements were run in triplicate for each film. Tensile strength is the maximum stress applied to a point at which the film specimen bursts.

Moisture absorption: Films of each formulation were accurately weighed and exposed to ambient atmospheric conditions of temperature (avg. temp 34 ^{0}C) and humidity (75 %) for three days. After three days, the films were again weighed and percentage moisture absorption was calculated.

In vitro drug release studies: The optimized films of known weight and dimension (3 X 23cm) were placed in a beaker containing 100ml of phosphate buffer (pH 7.2) as the dissolution medium maintained at 37±0.5°C. The medium was stirred at 100 rpm. Aliquots (5 ml) of samples were taken at 5sec time intervals, and the same volume of fresh phosphate buffer was replaced. Samples were filtered, diluted suitably and analysed using UV/Visible spectrophotometer (V-630, JASCO, Japan) at λmax 263 nm. The cumulative percentage drug release was calculated and plotted against time (sec).[15]

RESULTS AND DISCUSSION

Visual Inspection: The transdermal films formulated with different polymer concentration were found to be flexible, smooth, opaque, sticky and homogeneous. This may be due to the presence of plasticizer.

Film Thickness: As the concentration of polymer and plasticizer increased the thickness of the film found to be increased. The film's thickness appears ideal and suitable for topical application.

Weight Variation: All the prepared formulations were uniform in weight with no significant difference in the weight of the individual formulations from the average value. Weight variation was found to be in the range of 0.89 ± 0.0115 to 0.96 ± 0.0152 gm for films prepared.

Drug Content: The percentage drug content in various formulations ranged from 80.00 % – 90.00 % and the drug content was found to be in the limit.

Folding Endurance: All the nine films have showed good folding endurance, It was observed that the folding endurance of the films increased with increase in the concentration of polymer and plasticizer. The flexibility of the films increased with increase in folding endurance.

Tensile Strength: Tensile strength gives an indication regarding strength and elasticity of the films. The effect of concentration of polymers on the tensile strength found that as the concentration

of polymer increased the tensile strength was also increased. This may be due to soft and tough nature of polymers

Moisture absorption: There was change in the Moisture absorption of all the formulation with increase in the concentrations of polymers.

***In vitro* drug release study:** The release of the drug from the formulation depends upon the type of polymer used. Formulation F1- F3 showed lesser drug release compared to other then maximum drug release from these formulation 89.62% where as other formulation maximum drug release 94.1%. Trigonelline hydrochloride is a water soluble compound present in fenugreek seed extract therefore as the concentration of hydrophilic polymer used in patch increased drug permeation through the patches increased and the effect of other non- polar content in fenugreek seed extract was reduced. Those formulations containing higher concentration of polymer showed increased drug release.

CONCLUSION

In the present study Transdermal patches of Fenugreek seed extract were successfully developed which offers a suitable and practical approach in serving desired objective of diabetes mellitus and improving bioavailability and patient compliance. The prepared formulations were evaluated using different parameters and they exhibited acceptable physical characteristics with good flexibility, folding endurance, tensile strength and percentage elongation. *In vitro* drug release have revealed that the formulation were suitable for the transdermal drug delivery system of the antidiabetic constituent (Trigonelline fenugreek seed extract) the substantial permeation of trigonelline through the artificial membrane indicate that if these formulation were used *in vivo* we can express some degree of antidiabetic activity. However, such a conclusion can be confirmed only by well design *in vivo* studies for antidiabetic activity. Based on the encouraging results, the Fenugreek seed extract transdermal patch can be used as controlled drug delivery system and frequency of administration can be minimized. Though the efforts were made for the development of Fenugreek seed extract transdermal patch, long term pharmacokinetic and pharmacodynamic studies are needed to undertake the establishment of the usefulness of these patches. Thus, the specific objectives listed in this thesis were achieved, namely evaluation of transdermal patches of Fenugreek seed extract. Further, these findings may help the industry to scale up for commercial production. Therefore. this study was to formulate fenugreek seed extract as a transdermal drug delivery system can be an effective drug delivery system for its systemic action in the treatment of diabetes mellitus. It also offers an advantage of controlled release from a transdermal drug delivery system with better therapeutic efficacy, improved patient compliance over the conventional drugs delivery system.

Table 1: Composition of transdermal films containing fenugreek seed extract

Formulation code	Fenugreek seed extract (g)	HPMC E15 LV (g)	HPMC 15cps (g)	HPMC 50cps (g)	Propylene glycol (ml)	DMSO (ml)	Ethanol (ml)	Distilled water upto (ml)
F1	2	1.5	-	-	1.5	0.5	20	50
F2	2	2	-	-	1.5	0.5	20	50
F3	2	2.5	-	-	1.5	0.5	20	50
F4	2	-	1.5	-	1.5	0.5	20	50
F5	2	-	2	-	1.5	0.5	20	50
F6	2	-	2.5	-	1.5	0.5	20	50
F7	2	-	-	1.5	1.5	0.5	25	50
F8	2	-	-	2	1.5	0.5	25	50
F9	2	-	-	2.5	1.5	0.5	25	50

Table 2: Evaluation parameters of transdermal films

Formulation code	*Thickness (mm.)	*Weight Variation (gm)	%Moisture Absorption	* Folding Endurance	* Tensile Strength (kg/cm2)
F1	0.35 ± 0.0115	0.91 ± 0.0153	2.62 ± 0.22	160 ± 10	1.0 ± 0.031
F2	0.36 ± 0.0153	0.93 ± 0.0058	3.6 ± 0.37	160 ± 10	1.1 ± 0.034
F3	0.37 ± 0.0058	0.93 ± 0.0100	4.4 ± 0.21	160 ± 12	1.3 ± 0.012

F4	0.33 ± 0.0115	0.89 ± 0.0115	3.2 ± 0.31	160 ± 10	1.0 ± 0.023
F5	0.39 ± 0.0058	0.90 ± 0.0173	4.44 ± 0.41	160 ± 11	1.2 ± 0.032
F6	0.40 ± 0.0100	0.94 ± 0.0208	4.7 ± 0.22	160 ± 10	1.3 ± 0.021
F7	0.36 ± 0.0153	0.93 ± 0.1528	3.41 ± 0.35	200 ± 12	1.3 ± 0.021
F8	0.39 ± 0.0056	0.94 ± 0.0204	4.6 ± 0.32	200 ± 10	1.5 ± 0.041
F9	0.41 ± 0.0152	0.96 ± 0.0152	5.12 ± 0.21	200 ± 15	2.0 ± 0.032

* Each reading is an average of 6 determinations

Table 3: Evaluation parameters of transdermal films

Formulation code	Drug content uniformity* %	% Cumulative drug release*
F1	82.50 ± 0.5127	85.34 ± 0.09
F2	84.96 ± 0.5714	88.7 ± 0.12
F3	87.62 ± 0.4015	89.62 ± 0.10
F4	85.40 ± 0.4670	84.53 ± 0.12
F5	86.68 ± 0.5321	91.02 ± 0.08
F6	86.81 ± 0.7481	93.91 ± 0.04
F7	83.41 ± 0.5104	87.02 ± 0.06
F8	85.78 ± 0.5132	92.41 ± 0.04
F9	89.91 ± 0.7345	94.1 ± 0.03

*Each reading is an average of 6 determinations

Figure 1: Cumulative percentage of drug release F1 to F3

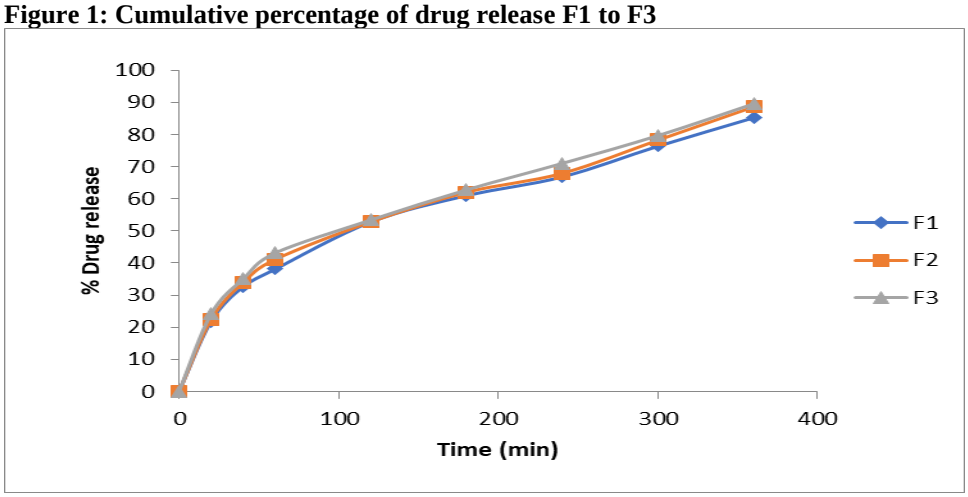


Figure 2: Cumulative percentage of drug release F4 to F6

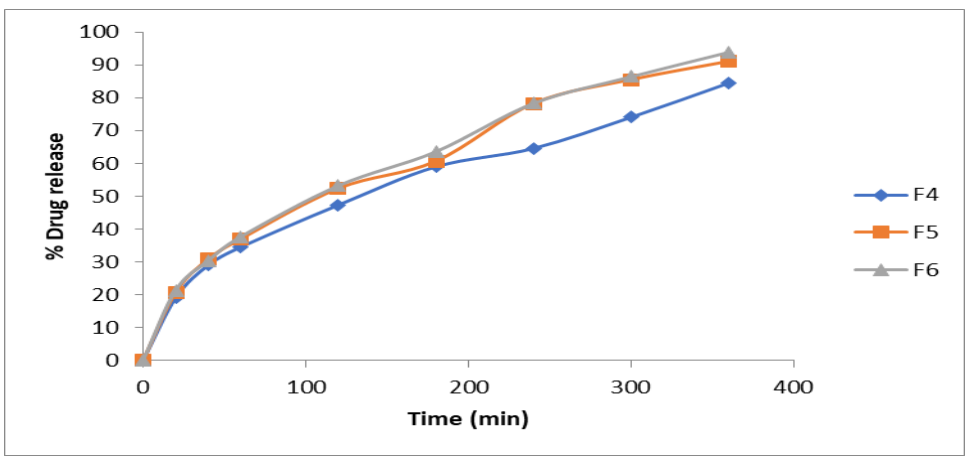


Figure 3: Cumulative percentage of drug release F7 to F9

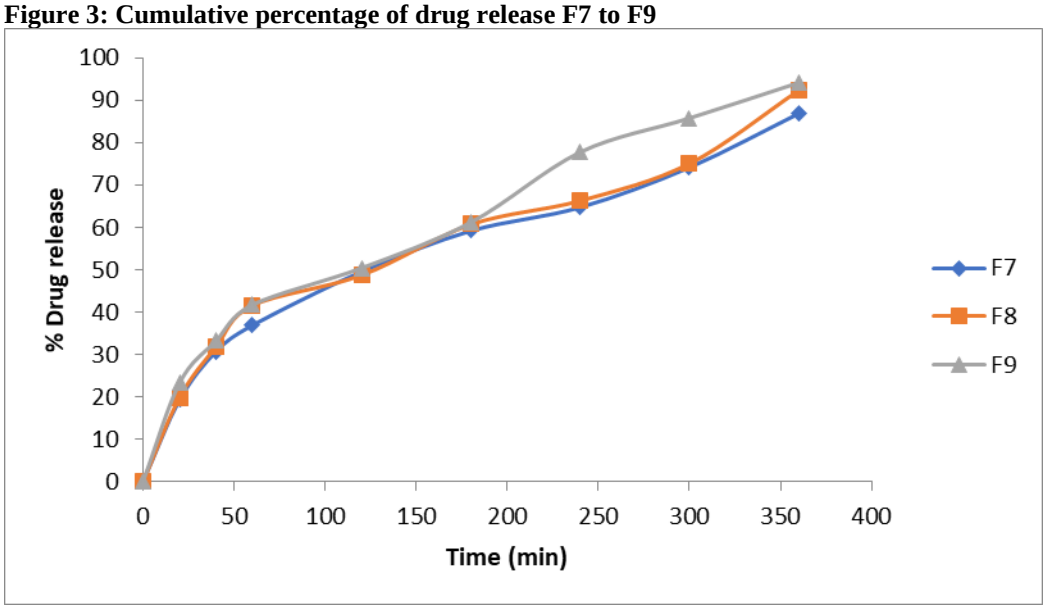


Figure 4: Casting solution in petri-plate

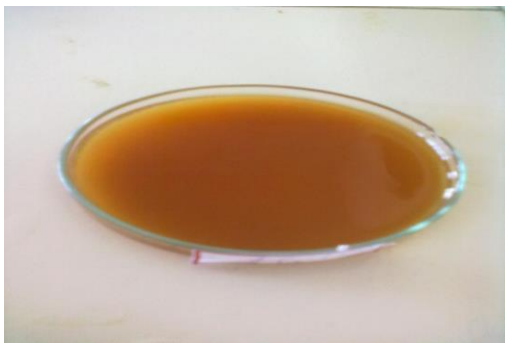
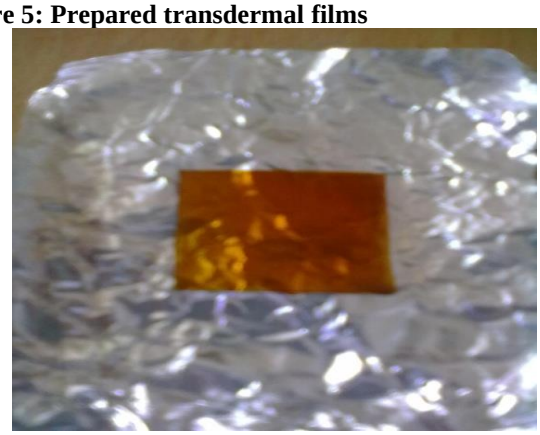


Figure 5: Prepared transdermal films



REFERENCES

1. Thomas G, Mohammed FH. Diabetes- The preventable epidemic. J Young Pharm. 2002; 5:1-11.
2. Baskaran K, Hasan SA. Antidiabetic effect of leaf extract from gymnema sylvestre in non- insulin dependent diabetes mellitus patients. Pharma Res. 1990; 30(3):295-300.
3. Chandalia M, Gilliyan CA. Benificial effect of high dietary fiber intake in patients with type 2 diabetes mellitus. J Young Pharma. 2003; 19:392-398.
4. Wehash FE, Ismail I. Some Physiological effect of momordica charantia and Trigonella foenum graceum extract in diabetic rat as compared with cidophage. J Pharma Sci Res. 2012; 64:4-21.

5. Gadekar R *et al*. Study of formulation, characterization and wound healing potential of transdermal patches of curcumin. Asian J Pharm Clin Res. 2012; 4(5): 225-230.
6. Yadav SK *et al*. Formulation and evaluation of transdermal patches for Antirheumatic Ayurvedic Medicine using different polymer composition. Int J Pharm Sci 2013; 4(1): 999-1006.
7. Aktar N *et.al*, Effect of cream formulation on some mechanical parameters of human skin. T J Pharm Res. 2010; 9(4): 329-337.
8. Rathva SR *et al*. Transdermal herbal patchaes. Int J Pharm Sci. 2012; 2(2): 397-402.
9. Sauvaire Y *et.al*. 4-Hydroxyisoleucine: a novel amino acid potentiator of insulin secretion. Int J Pharm Sci.1998; 4(7): 206-210.
10. Dholi SK *et al*. Invivo Antidiabetic evaluation of fenugreek seeds extract in Alloxan Induced Rats. Int Cur Sci Res. 2011; 1(3): 96-104.
11. Bolzinger MA *et al*. Penetration of drugs through skin, a complex rate- controlling membrane. Current Opinion in Colloid & Interface Science. 2010; 17 (3):156-165.
12. Keleb E *et al.* Transdermal drug delivery system – Design and evaluation. Int J Adv Pharm Sci. 2010; 1:201-211.
13. Gaur PK *et al*. Transdermal drug delivery system- A review. Asian J Pharm Cli Res. 2009; 2:14-20.
14. Finin BC, Morgan TM. Transdermal permeation enhancers: application, limitations and potentials. Indian J Pharm Sci .1999; 88(10):955-957.
15. Rohini RM *et al*. Diuretic effect of trigonella foenumgraecum seed extract. Int J Pharm Sci. 2009; 6(2): 1540-2584.