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Effect of Permeation Enhancer on Bioavailability of Formulated Patches of Glibenclamide

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ABSTRACT

Objectives: The objective of this study is to extract Phytochemical constituent from Cinnamon Bark and to design and develop the transdermal patch of the herbal drug along with modern medicine Glibenclamide using solvent casting method to reduce the dose required to obtain same pharmacological the effect, also to reduce the toxicity of the drug. **Methods:** The Glibenclamide Transdermal patches were formulated by using the solvent casting method. The physical and chemical similarity of the medication and the base of patches were studied by Infrared Spectroscopy (FTIR). The outcomes recommended no physical and chemical properties incongruence between the medication and the patch base. The formulated transdermal patches were assessed for the weight difference, fatness, folding endurance, wetness, moisture captivation, *ex vivo* drug release, *ex vivo* drug absorption. **Results:** The diffusion examines were performed by utilizing the Franz diffusion cell and everted gut sac method. The best formulation F5 showed Thickness 0.230±0.009mm, Weight uniformity 0.170±0.021gm, % Moisture uptake 8.307±1.00 Moisture content 5.045±0.214, % Drug content 80.80±0.091, Folding endurance27±4.50. Formulation F5 exhibits the highest % cumulative drug release 67.90±1.01% in 8hrs and highest %Drug absorbed 4.263±0.41 in 120 min. **Conclusion:** It can be concluded the formulation no. F5 shows maximum bioenhancing action compared to all other patches which contains Glibenclamide along with the Ethanolic extract of the Cinnamon bark.

Key words: Glibenclamide, Cinnamon bark, Folding endurance, *Ex vivo*, Phytochemical.

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INTRODUCTION

Bioavailability is the beat and level to which a restoratively unique substance enters central scattering and gets accessible at the essential site of movement. Intravenous meds accomplish the best bioavailability, while it was seen that oral association yields a reduced rate as a result of fragmented medicine absorption and first-pass metabolism.[1] Three fundamental points in particular solvency, disintegration, and intestinal porousness, influencing oral medication assimilation can be assessed utilizing the biopharmaceutics characterization framework (BCS). It arranges the medication into four classes: Type I (great solvency, great penetrability), Type II (little dissolvability, great porousness), Type III (great dissolvability, little porousness), and Type IV (little solvency, little penetrability). A portion of the ordinarily utilized anti-infection agents falls into Class III and Class IV classification as per this framework.[2] Diabetes is a chronic metabolic disorder in which there is hyperglycaemia caused by insulin deficiency this Glibenclamide is very potent administered orally to treat this condition.[3] Transdermal medication distribution system has many benefits above conservative modes of administration of drugs above the absorption of the drug.[4] Consistent and long-term Concentration of medicament can be achieved by transdermal drug delivery system.[5] In 1982 only US FDA approved Scopolamine transdermal film for motion sickness which is developed by GlaxoSmithKline.[6] USA has approved more than 35 transdermal delivery products for a wide variety of pathophysiological condition.[7] TDDS offers numerous benefits over the regular dose structures and oral controlled delivery conveyance frameworks, strikingly shirking of hepatic first-pass digestion, the decline in recurrence of organization, decrease in gastrointestinal results, and improves patient consistence.[8] These days, an examination into transdermal medication conveyance has extraordinarily expanded in the course of recent years. One of the main impetuses for this development is the expanding number of medications that can be conveyed to the fundamental flow in clinically successful fixation by means of the skin entryway. This has been conceivable in view of the amazing accomplishments of drug technologists who have not just made the transdermal conveyance framework as the best non-oral foundational drug conveyance framework yet in addition made its assembling a profoundly effective advertisement adventure.[9] Transdermal route of administration is the best route for long-term and frequent use of drugs for maintaining plasma concentration. [10]

MATERIALS AND METHODS

Materials

Glibenclamide was gotten as a free sample from Leben Laboratories Pvt. Ltd. Akola (MH) and other ingredients were obtained from Research lab Mumbai. The entire ingredient obtained was analytical grade. Materials Cinnamon bark, was obtained from local market, impurities and foreign material was inspected then removed and Authenticated from botanist. Cinnamon Bark consists of dehydrated bark inside bark of *Cinnamomum zeylanicum* Nees, belonging to family Lauraceae.[11,12] Cinnamon Bark contains 0.5 to 1.0% of volatile oil, 1.2 % of tannis mucilage, calcium oxalate, starch and a sweet substance is known as mannitol and is used for gastric trouble, loose motion, and has anti flatulence. It is also used for increasing appetite; it acts as antibacterial and anti-parasites.

Successive Solvent Extraction

Cinnamon Bark was extracted by means of successive hot extraction method by using Soxhlet apparatus in order to find out which extract shows the maximum Bio enhancing activity. Extraction was done in following manner

1) Chloroform, 2) Butanol, 3) Methanol, 4) Ethanol 5) Aqueous

Preparation of all extracts by successive extraction method all plant material were air dehydrated in shade in order to get consistent weight. The dehydrated samples of all plant material were ground later to rough powder. Fifty grams of crude powder of bark were taken in Soxhlet apparatus. Successive extraction with different solvents (Chloroform, Butanol, Methanol, Ethanol, and Aqueous) was carried out. Extracts were actuality sifted using funnel and Whatman No. 1 filter paper. Each remainder will be concerted to aridness under condensed pressure at 40°C through evaporator and stored at 4°C for further studies.[13,14]

Preformulaion Studies

Drug, Extract and Polymer compatibility: Fourier-change infrared spectroscopy (FTIR) was utilized to examine the unadulterated medication Glibenclamide, actual blend of Glibenclamide, and HPMC, PG, PEG 400, Glycerine, and ascorbic acid for any medication polymer interaction by KBr pellets technique. All samples were examined at Range: 4000 – 650

Standard Curve of Glibenclamide: Stock solution of Glibenclamide was prepared by dissolving 100 mg of Glibenclamide in 100 ml the standard volumetric flask containing 50 ml of phosphate buffer 7.4 and then the volume was made up to the mark with phosphate buffer 7.4 to obtain a concentration of 1000 µg/ml. Subsequent dilutions of this solution were made with mobile phase to obtain the concentration range of 5- 50 µg/ml. The standard solutions prepared as above were used to obtain a calibration curve in order to find the unknown concentration of Glibenclamide, for further study (Figure 1).[15]

Formulation and Development of Transdermal Patches: Transdermal patches were set up by dissolvable solvent casting method. HPMC was weighed precisely and included 3 ml of distil water. The substance in the beaker was blended on magnetic stirrer for 15 min for swelling of the polymer. At that point Propylene glycol was added to the polymer solution. 100mg Glibenclamide was weighed and dissolved in 2 ml of distilled water. The medication arrangement was added to the polymer dispersion and Citric acid was blended altogether with the assistance of magnetic stirrer. At that point after complete mixing solution was allow to stand for 20 min to ensure the removal of air bubbles. Afterward it was poured consistently in Petri dishes and was left for 24hr at room temperature for drying. Subsequent to drying after 24hr patches were taken out by stripping from the Petri dishes at that point cut into a square component of 2× 2 cm. Patches were stuffed in aluminium foil and put away in a water/air proof holder to keep up their trustworthiness and versatility. The compositions of the various formulations of glibenclamide and extracts are listed in Tables 1, 2.[16,17]

Evaluation of Transdermal Delivery Patches

The Physicochemical evaluation of transdermal patches are based on following parameters

Thickness of patch: The thickness of each transdermal film was estimated by utilizing a screw check at five distinct places of the film and the mean worth was determined.[18]

Weight uniformity: Film sizes of 2cm radius (4cm diameter) were cut. The masses of five film were taken and the weight difference was intended.[19]

Folding endurance: A film of 2cm range (4cm measurement) cut uniformly and more than once folded at a similar spot till it brakes. The quantities of times the film were collapsed at a similar spot without breaking given the estimation of the folding endurance.[20]

Percentage moisture content: The formulated patches were weighed separately and reserved in a desiccators containing fuse calcium chloride at room temperature for 24h. After 24h, the patches were weighed and determined the fraction moisture content from the formula.[21]

Percentage moisture uptake: The weighed patches were reserved in desiccators at room temperature for 24h comprising saturated solution of potassium chloride in order to maintain 84% RH. After 24h, the patches were reweighed and determined the percentage moisture uptake from the formula.[22]

Drug content: A particular area of film was dissolved in a phosphate buffer solution. The content was stirred to dissolve the transdermal patch. The content was relocated to a volumetric flask. The absorbance of the solution was measured and content of drug was determined.[23]

Bioenhancing Activity Model

A) *Ex vivo* Permeation Study: Goat Skin was obtained from the local market and treated properly. *Ex vivo* permeation studies were performed on Franz diffusion cells with an effective sectional area of 3.14 cm^2 and 15 ml of receiver chamber capacity. The treated goatskin was cut into the desired size and placed between the receptor and donor compartments of the diffusion cell. The patch was placed over the membrane. The donor

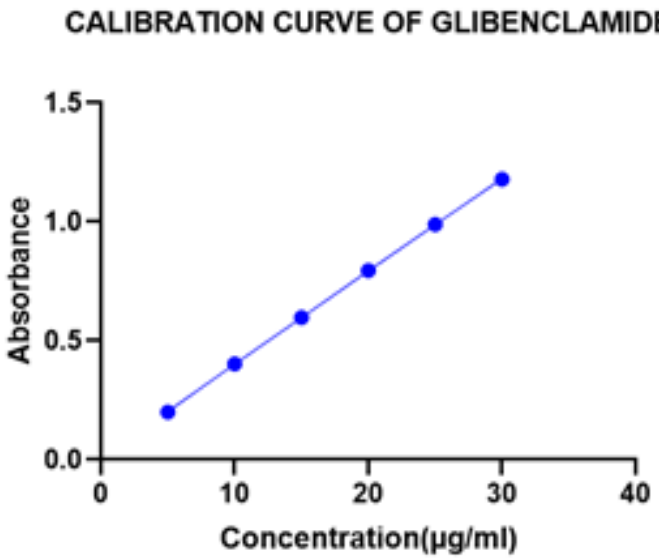

Figure 1: Calibration curve of Glibenclamide.[15]

Table 1: Composition of patches formulation code.

Formulation code	Content
F1	Glibenclamide
F2	Glibenclamide+ Cinnamon Chloroform Extract
F3	Glibenclamide+ Cinnamon Butanolic Extract
F4	Glibenclamide+ Cinnamon Methanolic Extract
F5	Glibenclamide+ Cinnamon Ethanolic Extract
F6	Glibenclamide+ Cinnamon Aqueous Extract
F49	Glibenclamide + HPMC+PG+ PEG 400+ Glycerine +Citric Acid

compartment was placed on the receptor compartment containing phosphate buffer PH 7.4 maintained at 37± 0.5°C and the clamp is placed in between the donor compartment and receptor compartment for fixing them together entire assembly was kept on a magnetic stirrer. The solution in the receiver compartment was uninterruptedly stirred with magnetic beads. The amount of the drug infused through the membrane was determined by withdrawing the particular amount of the sample at programmed time intermission and substituting them with an equivalent volume of phosphate buffer. The absorbance of the samples was taken with the help of a spectrophotometer.[24-26]

B) **Everted Gut Sac Model:** Goat's small intestine was obtained from slaughtering houses from the local market. The intestine was transported in buffer solution and obtained into two pieces of 15cm each; the estimated diameter of the intestine was 0.7 cm. One end of the intestine was tied up and everted with the help of a glass rod; the cannula was connected to another end of the intestine in order to form the pouch and added a small volume of drug-free buffer solution. Continuous supply of oxygen was provided to the tissue in order to keep it alive with the help of an oxygen pump and phosphate buffer solution; the temperature was continued at 37± 0.5°C throughout the entire procedure. After eversion, the mucosal side came out and the serosal side was present inside. The stratum corneum side of the skin was kept in close contact with the release surface of the transdermal patch. At a predetermined time the sample from the sac was removed and the concentration of the drug in a serosal fluid was determined with the help of a spectrophotometer. Finally, % of absorbance was calculated against time.[27,28]

RESULTS

All the formulated patches successfully worked subjected to diffusion study which is supported out with the help of the Franz diffusion cell method and everted gut sac model. Samples were collected at predetermined time and absorbance of every sample was measured with the help of spectrophotometer in order to find out the %of drug content. The result of the diffusion studies has been discussed in graph by plotting time in X-axis and cumulative % release in Y-axis as well as % absorbance against time in case of Everted Gut Sac Model. During this study it has been found that natural bioenhancers like cinnamon bark extract can be used along with modern medicine like Glibenclamide in order to expand bioavailability of drug through transdermal drug delivery system.

Compatibility studies of drug and extract as well as drug and polymers were studied with the help of FTIR shows no drug extract and drug polymer interaction, result of which shown in Figures 2 to 8. Physicochemical parameters like % moisture content, thickness, weight variation etc. are within limit shown in Table 3. The results of *ex vivo* permeability studies and everted gut sac studies were mention in Table 4 and Table 5, respectively.

Amongst all the extracts Ethanolic extract (F5) showed significant increase in % CDR 67.90 as well as in % drug absorbance 4.26.

Order of permeation enhancing effect Franz Diffusion cell studies

F5>F3>F4>F2>F6>F1

Order of % drug absorption in case of Everted Gut Sac model

F5>F4>F3>F2>F6>F1

From all above study it was observed that extract of cinnamon bark along with the modern medicine showed great bioavailability compared to Glibenclamide alone.

DISCUSSION

Long term treatment and multidrug therapy can be overcome by use of the transdermal drug delivery system which in turn increases bioavailability of drug by avoiding first pass metabolism which destroy the maximum amount of the drug. Drug directly reaches to the systemic circulation and increases the therapeutic efficacy. Glibenclamide is a potent antidiabetic drug used widely for the treatment of type-II diabetes.

But because of first pass metabolism it shows less therapeutic effect. Polymers such as HPMC, PEG selected as it showed good adhesive activity and better skeleton formation which is the base of transdermal patches. Phosphate buffer with pH 7.4 was used to find out the solubility of drug and also to find out the unknown concentration of the drug. FTIR was done to find out the drug-polymer and drug-herbal extracts

Table 2: Optimized formulation design for cinnamon bark extracts with glibenclamide.

Ingredients	FORMULATION CODE					
	F1	F2	F3	F4	F21	F6
Glibenclamide	100mg	100mg	100mg	100mg	100mg	100 mg
HPMC	400 mg	400 mg	400 mg	400 mg	400 mg	400 mg
PG	0.4ml	0.4ml	0.4ml	0.4ml	0.4ml	0.4ml
PEG-400	0.4ml	0.4ml	0.4ml	0.4ml	0.4ml	0.4ml
Citric Acid	10mg	10mg	10mg	10mg	10mg	10mg
Water	Up to 5ml	Up to 5ml	Up to 5ml	Up to 5ml	Up to 5ml	Up to 5ml
Chloroform extract	-----	50mg	-----	-----	-----	-----
Butanolic Extract	-----	-----	50 mg	-----	-----	-----
Methanolic Extract	-----	-----	-----	50 mg	-----	-----
Ethanolic Extract	-----	-----	-----	-----	50 mg	-----
Aqueous extract	-----	-----	-----	-----	-----	50 mg

Table 3: Characterisation of patches formulation for thickness, weight uniformity, moisture and drug content.

Parameters	FORMULATION CODE					
	F1	F2	F3	F4	F5	F6
Thickness (mm)	0.221±0.008	0.218±0.007	0.214±0.009	0.234±0.006	0.230±0.009	0.228±0.103
Weight uniformity (gm)	0.180±0.009	0.176±0.006	0.170±0.005	0.177±0.003	0.170±0..021	0.172±0.033
% Moisture uptake	7.202±1.62	7.224±0.009	6.321±1.09	6.169±2.01	8.307±1.00	6.502±1.29
% Moisture content	4.776±0.543	4.12±0.926	4.55±0.636	4.434±0.207	5.045±0.214	6.045±0.214
% Drug content	79.2±0.63	72.84±0.084	74.89±0.34	82.74±0.02	80.80±0.91	80.92±0.45
Folding Endurance	20±2.63	22±2.80	19±302	25±3.33	27±4.50	23±3.39

*All data are presented in Average ± SD, *n*=3

Table 4: Release kinetic of formulation from studies Franz Diffusion cell.

Time in hrs.	Formulation Code					
	F1	F2	F3	F4	F5	F6
0.5	2.32±0.35	2.40±0.13	3.22±0.78	5.82±0.55	8.90±0.78	2.42±0.23
1.0	4.30 ±1.09	4.78±0.43	5.24±0.77	7.28±0.86	9.25±0.56	4.39±1.04
1.5	6.12±1.22	7.14±0.29	7.12±0.23	9.19±0.47	10.09±0.55	6.45±1.04
2.0	8.04±1.01	8.76±0.89	10.53±0.34	12.53±0.48	15.55±0.65	8.87±1.98
2.5	9.11±1.56	9.89±0.19	14.25±0.44	17.23±0.34	20.76±0.77	9.87±0.59
3.0	10.88±1.10	12.67±0.19	20.77±0.60	22.43±0.67	25.99±0.87	11.71±1.25
4.0	13.44±1.67	14.75±0.87	26.17±0.17	30.09±1.12	33.07±1.04	13.98±1.74
5.0	24.67±1.05	24.88±0.38	31.32±0.23	36.23±1.12	39.37±1.02	25.11±1.04
6.0	35.34±1.55	36.55±0.74	40.09±0.98	45.09±1.07	55.03±1.11	35.98±1.12
8.0	53.21±1.27	54.45±0.98	60.90±0.87	59.90±1.23	67.90±1.01	53.74±1.18

*All data are presented in Average ± SD, *n*=3

Table 5: Gut sac model of formulation.

Time in Min.	Formulation Code					
	F1	F2	F3	F4	F5	F6
10	0.542±0.12	0.590±0.41	0.601±0.11	0.611±0.14	0.647±0.55	0.552±0.71
20	0.982±0.17	1.121±0.21	1.171±0.19	1.245±0.17	1.310±0.43	0.987±0.84
30	1.231±0.41	1.277±0.39	1.348±0.22	1.554±0.12	1.774±0.12	1.235±0.14
60	1.591±0.22	1.782±0.12	1.975±0.14	2.810±0.32	2.977±0.34	1.611±0.19
90	1.842±0.14	2.273±0.17	2.694±0.52	3.481±0.25	3.541±0.74	1.851±0.29
120	2.104±0.15	2.643±0.56	3.217±0.71	4.101±0.21	4.263±0.41	2.114±0.72

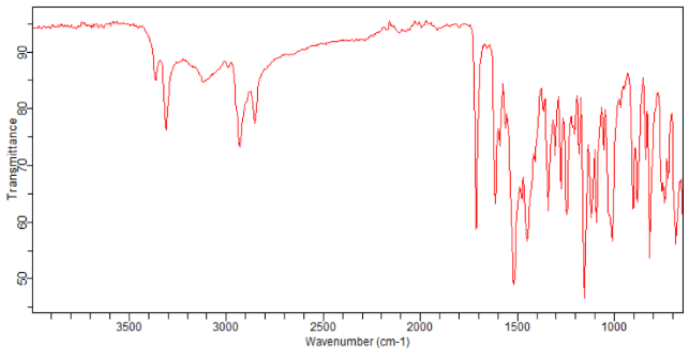

Figure 2: FTIR spectrum of Glibenclamide.

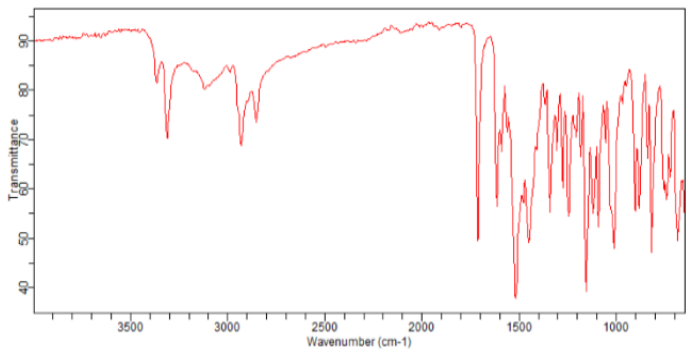

Figure 3: FTIR spectrum of Glibenclamide with Cinnamon Chloroform Extract.

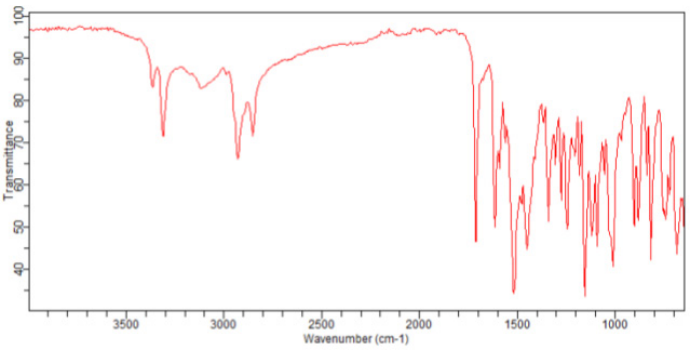

Figure 4: FTIR spectrum of Glibenclamide with Cinnamon Butanol Extract.

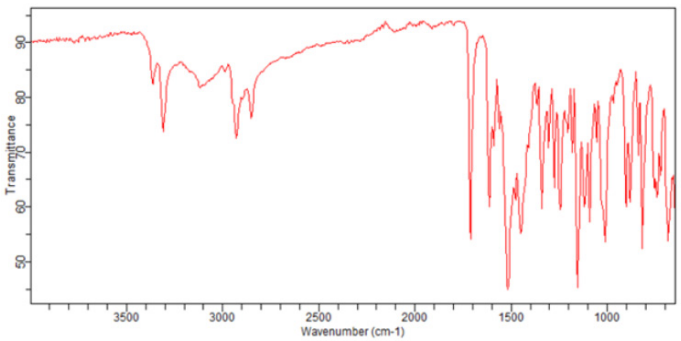

Figure 5: FTIR spectrum Glibenclamide with Cinnamon Methanolic Extract.

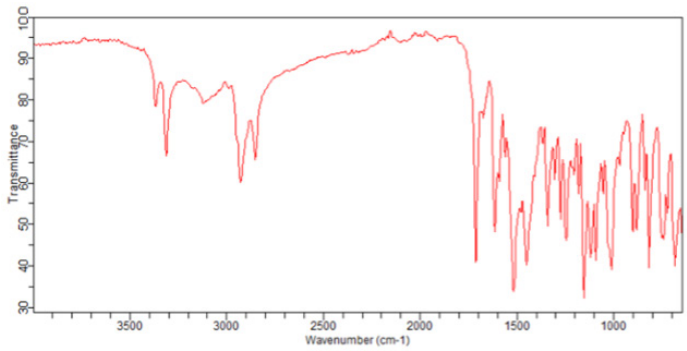

Figure 6: FTIR spectrum of Glibenclamide with Cinnamon Ethanolic Extract.

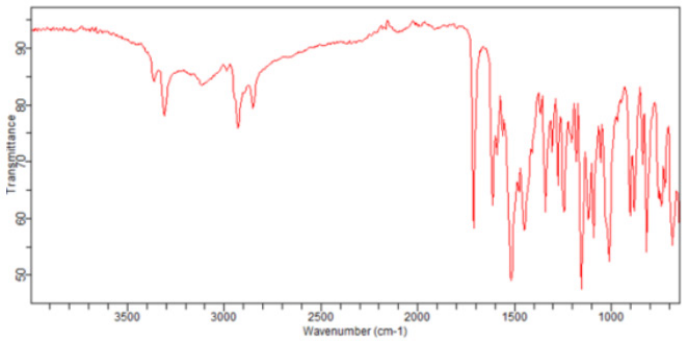

Figure 7: FTIR spectrum of Glibenclamide with Cinnamon Aqueous Extract.

compatibility. FTIR studies were performed on the pure bulk drug as well as on extract and polymer in order to get the stable formulation.

The formulated patches were subjected for various physical and chemical evaluation parameters in order to standardize the formulation. All

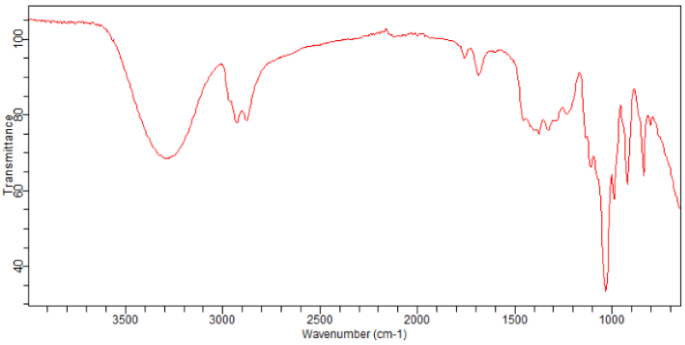

Figure 8: FTIR spectrum of Glibenclamide with polymer.

the evaluated parameters for various formulation comes under limit. Out of all the formulation, formulation number F5 showed improved bioavailability of Glibenclamide compared to rest of the extracts.[26]

CONCLUSION

It can be concluded that herbal drugs in the form of extract can also be used in formulating transdermal patches due to opportunity of release of drug formulation which is very novel approach. The Glibenclamide patches made by solvent evaporation technique comprising of different extract of Cinnamon bark along with Glibenclamide were formulated. The drug was found compatible with different extracts and the polymers. All extracts shows bioenhancing activity to some extent compared to individual Glibenclamide patch. Amongst all the formulations F5 shows significant increase in drug release and drug absorption. As an extension to this work *in vivo* studies and clinical research on human being can be carried out in future.

ACKNOWLEDGEMENT

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

TDDS: transdermal drug delivery system; **HPMC:** hydroxyl propyl methyl cellulose; **PG:** propylene glycol; **PEG:** Polyethylene glycol; **FTIR:** Fourier Transform Infrared Spectroscopy.

REFERENCES

1. Atal N, Bedi KL. Bioenhancers: Revolutionary concept to market. Jayurveda Integr Med. 2010;1(2):96-9.
2. Barve K, Ruparel K. Effect of bioenhancers on amoxicillin bioavailability. ADMET and DMPK. 2015;3(1):45-50.
3. Gupta JR, Irchhiaya R, Garud N, Tripathi P, Dubey P, Patel JR. Formulation and evaluation of matrix type transdermal patches of Glibenclamide. Int J Pharm Sci Drug Res. 2009;1(1):46-50.
4. Bhanja S, Rawat BS, Sudhakar M, Panigrahi BB. Design, development and evaluation of transdermal patches of ramipril. Int J Adv Pharm Biol Chem. 2014;3(2):352-60.
5. Agarwal S, Gautam G. Formulation, development and evaluation of atorvastatin ethosomal gel. Int J Pharm Inv. 2020;10(4):452-5.
6. Jabbar AS. *In-vitro; ex-vivo* assessment of anti-inflammatory Tapentadol loaded non-ionic surfactant vesicular systems for effective transdermal delivery. Sys Rev Pharm. 2020;11(12):636-43.
7. Amandeep S, Alka B. Formulation and characterization of transdermal patches for controlled delivery of duloxetine hydrochloride. J Anal Sci Technol. 2016;7(2):2-13.

8. Mamatha T, Venkateswararao J, Anitha N. Development and physicochemical, *in vitro* and *in vivo* evaluation of transdermal patches of zaleplon. Indian J Educ Res. 2013;46(4):49-58.
9. Dhanalakshmi S, Harikrishnan N, Devi M, Keerthana V, Vijayalakshmi. Fabrication and evaluation of herbal transdermal film from *Hibiscus-rosa sinensis*. Int J Curr Pharm. 2019;11(5):101-5.
10. Umekar MJ, Biyani DM, Amgaonkar YM, Bhoyar PK, Lade UB, Kalsait RP. Formulation development and evaluation of transdermal drug delivery system of antihypertensive drug. Res J Pharm Tech. 2010;3(3):1-8.
11. Kokate CK, Purohit AP, Gokhale SB. Text Book of Pharmacognosy Nirali Prakashan 51st Edition. 2016;P14.124, 14.25 and 14.39.
12. Singh R, Parasuraman S, Kathiresan S. Antioxidant and antidiabetic activities of methanolic extract of bark of *Cinnamomum zeylanicum* in diabetic rats. Free Radic Antioxid. 2020;10(1):16-23.
13. Paliwal R, Madungurum MA, Dahiru N. Phytochemical analysis, physiochemical activity and antibacterial effects of *Cinnamon zeylanicum* (dalchini) extracts. Int J Eng Sci Res Tech. 2018;7(4):162-70.
14. Yessuf AM. Phytochemical extraction and screening of bio activecompounds from black cumin (*Nigella Sativa*) seeds extract. Am J Life Sci. 2015;3(5):358-64.
15. Mutalik S, Udupa N. Formulation development, *in vitro* and *in vivo* evaluation of membrane controlled transdermal systems of glibenclamide. J Pharm Pharm Sci. 2005;8(1):26-38.
16. Chavan S, Salunkhe P, Mohite N, Shinde C. Formulation and evaluation of oral fast dissolving film. Int J Curr Adv Res. 2019;8(6):19028-30.
17. Yadav PK, Mishra S. Transdermal patch of an antihypertensive drug: its development and evaluation. World J Pharm Res. 2017;6(4)1355-74.
18. Hanumanaik M, Patil U, Kumar G, Patel SK, Singh I, Jadatkar K. Design, evaluation and recent trends in transdermal drug delivery system: A review. Int J Pharm Sci Res. 2012;3(8):2393-406.
19. Kriplani P, Sharma A, Aman PP, Chopra B, Dhingra A, Deswal G. Formulation and evaluation of transdermal patch of diclofenac sodium. Glob J Pharm Pharm Sci. 2018;4(4):1-4.
20. Prabhu P, Shah S, Gundad S. Formulation development and investigation of domperidone transdermal patches. Int J Pharm Inv. 2011;1(4):240-6.
21. Premjeet S, Bilandi A, Sahil K, Akanksha M. Transdermal drug delivery system (patches), applications in present scenario. Int J Res Pharm Chem. 2011;1(4):1139-51.
22. Raza R, Mittal A, Kumar P, Alam S, Prakash S, Chauhan N. Approaches and evaluation of transdermal drug delivery system. Int J Drug Dev Res. 2015;7(1):222-33.
23. Idrees A, Rahman NU, Javaid Z, Kashif M, Aslam I, Abbas K, *et al. In vitro* evaluation of transdermal patches of flurbiprofen with ethyl cellulose. Acta Pol Pharm. 2014;7(2):287-95.
24. Shankar SJ, Kapadiya PP, Prabhu M, Raju PB. Formulation and evaluation of transdermal patches of an antidiabetic drug of glibenclamide. World J Pharm Sci. 2015;5(1):522-41.
25. Srilakshmi A, Teja VR, Lakshmi K, Thippesh M, Salma SU, Nagendrababu B. Formulation and evaluation of transdermal patches of Irbesartan. Indian J Res Pharm Biotechnol. 2017;5(3):212-5.
26. Kumar YP, Saurabh M. Transdermal Patch of an antihypertensive drug: It's development and evaluation. World J Pharm Res. 2017;6(4):1355-74.
27. Shen JY, Yang XL, Yang ZL, Kou JP, Li F. Enhancement of absorption and bioavailability of echinacoside by verapamil or clove oil. Drug Des Dev Ther. 2015;9:4685-93.
28. Luo Z, Liu Y, Zhao B, Tang M, Dong H, Zhang L, *et al. Ex vivo* and *in situ* approaches used to study intestinal absorption. J Pharmacol Toxicol Meth. 2013;68(2):208-21.

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