Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 10 [5] April 2021 : 146-155

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

ORIGINAL ARTICLE **OPEN ACCESS**

Formulation and Development of Transdermal Patches of Glibenclamide and Comparative Effect of Black Cumin Seed Extracts on *Ex Vivo* Release

Ashish Kandalkar*, Nitu Singh
Oriental College of Pharmacy and Research, Oriental University, Indore, M.P.45355 (INDIA)
Email: ashishkandalkar1@gmail.com

ABSTRACT

This study was mainly designed to formulate and evaluate transdermal patches of Glibenclamide by means of various polymers and to study the effect of extracts of Black Cumin seed on the bioavailability of Glibenclamide. 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 weight variance, corpulence, folding endurance, humidity, moisture captivation, ex-vivo drug release, ex-vivo drug absorption. The diffusion examines were performed by utilizing the Franz Diffusion cell and Everted gut Sac method. The best formulation F9 showed Thickness 0.247±0.005mm, Weight uniformity 0.127±0.029gm, % Moisture uptake 8.117±3.045,% Moisture content 6.147±0.324, % Drug content 84.56±0.098, Folding endurance25±3.33. Formulation F9 exhibits the highest % cumulative drug release 81.23±1.45% in 8hrs and highest %Drug absorbed 4.341±0.34 in 120 min.

Keywords: *Glibenclamide, Black Cumin seeds, FTIR, Moisture content, ex vivo*.

Received 02.01.2021 Revised 20.03.2021 Accepted 31.03.2021

INTRODUCTION

Glibenclamide 5-Chlor- N- (2- { 4- [(cyclohexylcarbamoyl) sulfamoyl] phenyl} ethyl)-2-methoxybenzamid Bioavailability is the beat and level to which a restoratively specific substance enters valuable scattering and receives on hand at the important web site of motion. Intravenous meds accomplish the fine bioavailability, while it became visible that oral affiliation yields a discounted fee because of fragmented remedy absorption and primary-bypass metabolism [1] Three essential point especially solvency, disintegration, and intestinal porousness, influencing oral remedy assimilation may be assessed using the bio pharmaceutics characterization framework, It arranges the medicine into 4 instructions: type i (extraordinary solvency, top notch penetrability), type ii (little dissolvability, super porousness), kind iii (brilliant dissolvability, little porousness) and sort iv (little solvency, little penetrability). A part of the in the main utilized anti-infection sellers fall into class iii and class iv classification as in step with this framework [2] Diabetes is persistent metabolic ailment in which there may be hyperglycaemia due to insulin deficiency for this Glibenclamide is a totally powerful administered orally to deal with this condition [3]. Transdermal medicine distribution gadget has many benefits above conservative modes of management of medication 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 authorised scopolamine transdermal movie for motion sickness that's developed through GlaxoSmithKline [6]. America has approved extra than 35 transdermal shipping products for wide type of pathophysiological condition [7]. TDDS provide numerous blessings over the everyday dose structures and oral controlled transport conveyance frameworks, strikingly shirking of hepatic first-pass digestion, the decline in recurrence of business enterprise, decrease in gastrointestinal consequences and improves affected person consistence [8]. Research in transdermal medication conveyance has especially expanded in the direction of recent years. One of the predominant impetuses for this development is the increasing wide variety of medicines that may be conveyed to the fundamental float in clinically successful fixation by means of the pores and skin entryway. This has been attainable in view of the exquisite accomplishments of drug technologists who've now not just made the transdermal conveyance framework because the satisfactory non-oral foundational drug conveyance framework yet in addition made its assembling a

profoundly effective advertisement adventure [9]. Transdermal route of administration is the first-rate direction for long time and frequent use of drug for keeping plasma concentration [10]. In view of the developing traits in the discipline of drug discovery, evaluation of the permeability traits of candidate drug molecules is an increasing number of turning into a important issue in studies undertaken in the course of lead selection and optimisation [11].

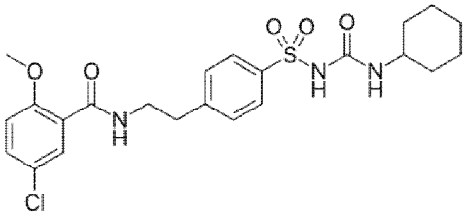

Fig. 1chemical structure of Glibenclamide

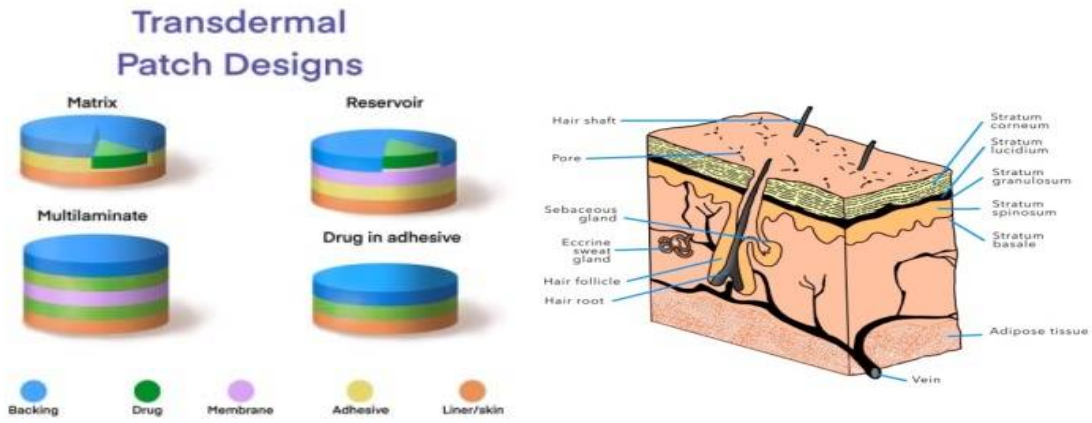

Fig. 2 TDDS patch and Skin

MATERIAL AND METHODS

Materials:

Drug & Chemical

Glibenclamide got as a free sample from Leben laboratories pvt. Ltd. Akola (MH) and different components were acquired from Research lab Mumbai. The entire ingredient obtained was of analytical grade.

Plant Material Used

Plant Materials Black Cumin Seed was obtained from local market impurities also foreign material is inspected then removed and Authenticated from botanist.

Black Cumin Seeds: [12]

Fig. 3 Black Cumin Seeds

Biological Source: It consists of dried seeds of Nigella sativa belonging to family Ranunculaceae.
Chemical Constituents: Carvone, Alpha Pinene, p-cymene, oleic acid.
Uses:. Improves appetite, Stimulant, Diuretic, Carminative, and used as Deodorant.
Successive Solvent Extraction [13,14]

Cumin seeds were extracted by using successive hot extraction method via using Soxhlet apparatus with a view to find out which extract shows the most bio enhancing interest. Extraction changed into performed in following manner

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

Preparation of all extracts by successive extraction method material was air dehydrated in shade so as to urge consistent weight. The dehydrated sample of all material was ground later to rough powder. Fifty grams of crude powder of black cumin was taken in Soxhlet apparatus. Successive extraction with different solvents (Chloroform, Butanol, Methanol, Ethanol, and Aqueous) was administered. Extracts were actuality sifted using funnel and Whatman No. 1 paper. Each remainder are going to be concerted to aridness under condensed pressure at 40°C through evaporator and stored at 4°C for further studies.

Preformulaion Studies

Melting point: Glibenclamide melted at 1700C.

Drug, Extract and Polymer Interaction

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 [15]:

Stock solution of Glibenclamide was produced in 100ml volumetric flask previously filled with 50ml of Phosphate buffer 7.4 and final volume marked up to 100ml with phosphate buffer 7.4 given concentration of 1000 µg/ml further dilutions were made to obtain concentration range of 5-50 µg/ml. The standard solutions prepared as above were used to obtain calibration curve in order to find the unknown concentration of Glibenclamide, for further study.

Formulation and Development of Transdermal Patches [16,17]

Transdermal patches were formulated by using solvent casting method with the help of various polymers. 3ml of distilled water was added to previously weighed HPMC. In order to swell polymer it was continuously stirred with magnetic stirrer for 15 min to form swelling. Polymer solution was then added with propylene glycol. Glibenclamide was weighed and added in 2ml of water. Polymer dispersion and drug solution was mixed properly followed by addition of citric acid. This solution was allowed for some time to remove the bubbles after that poured in petri dishes and left for 24 hrs at room temperature for proper drying. Very next day films were properly removed by peeling and square dimension of 2X2cm was obtained by cutting. Films were pack in aluminium foil and stored for further studies.

Evaluation of Transdermal Delivery Patches:

The Physicochemical evaluation of transdermal patches are based on following parameters

Thickness of patch [18]

For this study screw gauze check was done at 5 different points and average was taken.

Weight uniformity [19]

Random 5 films were selected and weighed properly to find out any weight variation.

Folding endurance [20]

It was calculated by folding the film at same sport until it breaks gives value for folding endurance.

Percentage moisture content [21]

Before and after weight of patches were calculated by using desiccator.

Percentage moisture uptake [22]

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.

Drug content [23]

A certain area of film was dissolved in a phosphate buffer solution. The contented 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.

Bioenhancing Activity Model:

Preparation of phosphate buffered saline pH 7.4 [7]

0.19 g of potassium dihydrogen phosphate, 2. 38 g of disodium hydrogen orthophosphate, and 8 g of NACL changed into weighed appropriately and dissolved in distilled water, subsequently the quantity become made up to 1000 ml with distilled water. The pH of the buffer changed into attuned to 7. 4.

A) **Ex-vivo Permeation Study** [24,25,26]

Goat skin was received from local market and handled properly. Ex vivo permeation research had been performed on Franz diffusion cells with an powerful sectional vicinity of 3.14 cm2 and 15 ml of receiver chamber ability. The treated goat pores and skin changed into reduce into preferred size and placed

among the receptor and donor booths of the diffusion mobile. The patch turned into located over the membrane. The donor compartment became positioned on the receptor compartment containing phosphate buffer pH 7. Four maintained at ± 0.5ºC and clamp is located in between donor compartment and receptor compartment for fixing them collectively complete set up kept on magnetic stirrer. The solution in the receiver compartment changed into uninterruptedly stirrer with magnetic beads. The quantity of the drug infused through membrane changed into decided by way of chickening out precise quantity of the sample at programmed time intermission and substituting them with an equal volume of phosphate buffer. The absorbance of the samples turned into taken with the help of spectrophotometer using phosphate buffer as the blank.

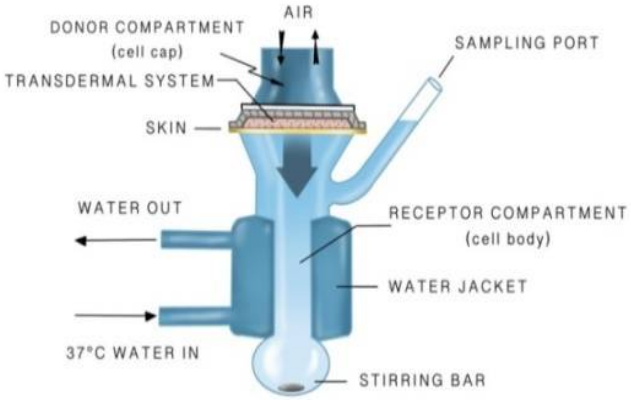

Fig.4 Franz Diffusion Cell

B) Everted Gut Sac Model [27,28]

Goat small intestine is acquired from slaughtering residence from neighborhood market. Which was then acquired in to 2 pieces of 15cm each; predicted diameter of intestine was 0.7 cm. One end the gut became tied up and everted with the assist of glass rod; cannula become connected to other end of the intestine as a way to shape as a pouch to which added small volume of drug free phosphate buffer. Continuous deliver of oxygen became provided to the tissue with a view to maintain it alive with the help of oxygen pump and phosphate buffer solution; the temperature becomes persevered at 37± 0.5oC through the entire technique. After eversion the mucosal side got here out and serosal aspect was internal. The stratum corneum facet of the skin changed into saved in near touch with the release floor of the transdermal patches. Absorbance was taken with the help of Spectrophotomete

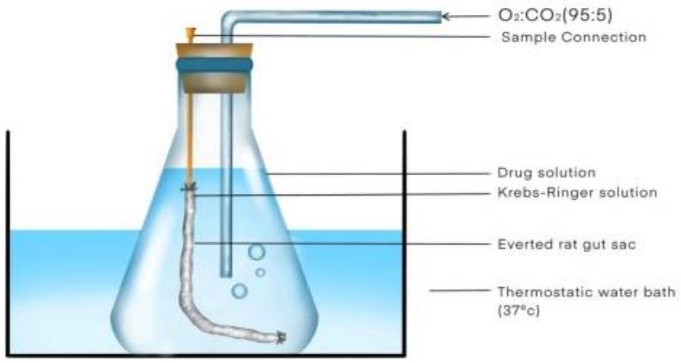

Fig.5 Everted Gut Sac Model

Table 1 Formulation Code

Formulation code	Content
F1	Glibenclamide
F7	Glibenclamide+ Black Cumin Seeds Chloroform Extract
F8	Glibenclamide+ Black Cumin Seeds Butanolic Extract
F9	Glibenclamide+ Black Cumin Seeds Methanolic Extract
F10	Glibenclamide+ Black Cumin Seeds Ethanolic Extract
F11	Glibenclamide+ Black Cumin Seeds Aqueous Extract
F49	Glibenclamide + HPMC+PG+ PEG 400+ Glycerine +Citric Acid

Table2 Standard curve of Glibenclamide

S.N	Concentration(µg/ml)	Absorbance
1	5	0.201
2	10	0.403
3	15	0.598
4	20	0.795
5	25	0.989
6	30	1.179

Table 3 Formulation Design for Black Cumin Seed Extract + Glibenclamide

Ingredients	FORMULATION CODE					
	F1	F7	F8	F9	F10	F11
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	-----	-----	50mg	-----	-----	-----
Methanolic Extract	-----	-----	-----	50mg	-----	-----
Ethanolic Extract	-----	-----	-----	-----	50mg	-----
Aqueous extract	-----	-----	-----	-----	-----	50mg

RESULT AND DISCUSSION

All the formulated patches efficiently worked subjected to diffusion examine which is supported out with the assist of the Franz diffusion cellular technique and Everted gut sac model. Samples have been amassed at predetermined time and absorbance of each sample becomes measured with the help of spectrophotometer which will discover the %of drug content. The result of the diffusion studies has been mentioned in graph by means of plotting time in x axis and cumulative % launch in y axis in addition to % absorbance against time in case of Everted gut sac version. At some point of this have a look at it has been discovered that herbal bioenhancers like cumin seed extract can be used in conjunction with contemporary medication like Glibenclamide with a purpose to increase bioavailability of drug.

1. 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 fig.7-13
2. Physicochemical parameters like % moisture content, thickness, weight variation etc are within limit shown in table 4
3. Ex vivo permeability studies are mention in table 5 and fig. 14
4. Everted Gut Sac studies are mention in table 6 and fig.15

Amongst all the extract Methanolic extract of Black Cumin Seed (F9) showed significant increase in % CDR as well as in drug absorbance.

Order of permeation enhancing effect Franz Diffusion cell studies

F9>F10>F8>F7>F11>F1

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

F9>F10>F8>F7>F11>F1

As an extension to this work In-vivo studies and clinical research on human being can be carried out in future.

Table 4 Evaluation of patches of Black Cumin Seed Extract + Glibenclamide

Parameters	FORMULATION CODE					
	F1	F7	F8	F9	F10	F11
Thickness (mm)	0.221±0.008	0.223±0.004	0.244±0.006	0.247±0.005	0.220±0.002	0.245±0.102
Weight uniformity (gm)	0.180±0.009	0.185±0.006	0.150±0.007	0.127±0.029	0.147±0.023	0.144±0.039
% Moisture uptake	7.202±1.62	8.242±1.044	7.112±1.055	8.117±3.045	9.307±1.977	7.787±1.345
% Moisture content	4.776±0.543	6.652±0.895	5.656±0.785	6.147±0.324	6.462±0.421	7.048±0.324
% Drug content	79.2±0.63	73.551±0.067	75.89±0.453	84..56±0.098	82.74±0.913	79.87±0.415
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 5 %CDR of Black Cumin Seed Extract + Glibenclamide patches

Time in hrs.	FORMULATION CODE					
	F1	F7	F8	F9	F10	F11
0.5	2.32 ±0.35	3.74 ±0.52	4.12 ±0.45	9.80 ±0.68	6.74 ±0.41	2.84 ±0.47
1.0	4.30 ±1.09	5.41 ±0.71	6.41 ±0.55	10.15 ±0.44	7.77 ±0.49	5.33 ±0.66
1.5	6.12 ±1.22	6.33 ±0.41	6.41 ±0.12	11.80 ±0.78	8.83 ±0.32	6.13 ±0.47
2.0	8.04 ±1.01	9.94 ±0.74	10.33 ±0.52	16.43 ±0.74	12.33 ±0.24	8.44 ±0.48
2.5	9.11 ±1.56	13.20 ±0.96	15.21 ±0.76	22.53 ±0.41	17.76 ±0.76	12.41 ±0.76
3.0	10.88 ±1.10	17.19 ±0.47	20.12 ±0.22	27.04 ±0.41	21.76 ±0.67	15.24 ±0.92
4.0	17.44 ±1.67	25.17 ±0.17	28.98 ±0.13	35.12 ±1.21	30.98 ±1.11	22.73 ±0.19
5.0	24.67 ±1.05	29.74 ±0.19	32.25 ±0.74	40.44 ±0.94	34.21 ±0.34	27.88 ±0.17
6.0	35.34 ±1.55	42.33 ±0.77	46.12 ±0.57	57.42 ±1.87	47.12 ±1.23	39.64 ±0.43
8.0	53.21 ±1.27	61.18 ±0.71	66.18 ±0.93	81.23 ±1.45	68.12 ±1.11	58.17 ±0.64

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

Table 6 %Drug absorbed of Black Cumin Seed Extract + Glibenclamide bulk drug

Time in Min.	FORMULATION CODE					
	F1	F7	F8	F9	F10	F11
10	0.542±0.41	0.614±0.11	0.614±0.65	0.771±0.88	0.622±0.91	0.550±0.74
20	0.982±0.75	1.290±0.42	1.290±0.42	1.422±0.41	1.311±0.19	0.997±0.91
30	1.231±0.12	1.521±0.78	1.521±0.22	1.947±0.73	1.728±0.27	1.245±0.25
60	1.591±0.24	1.711±0.44	2.456±0.49	3.127±0.57	2.911±0.31	1.710±0.29
90	1.842±0.34	2.155±0.74	3.255±0.77	3.872±0.19	3.655±0.95	1.849±0.37
120	2.104±0.87	2.333±0.27	3.823±0.91	4.341±0.34	4.122±0.88	2.112±0.74

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

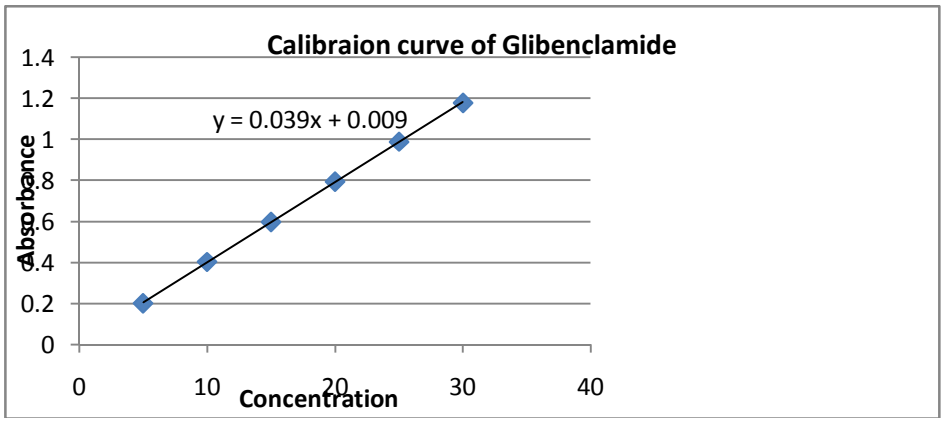

Fig. 6 Calibration curve of Glibenclamide

F1

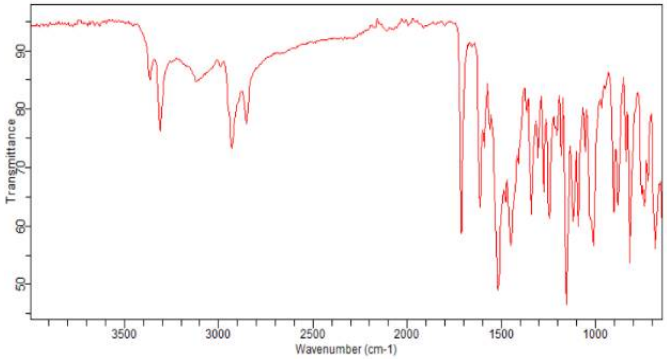

Fig. 7Glibenclamide

F7

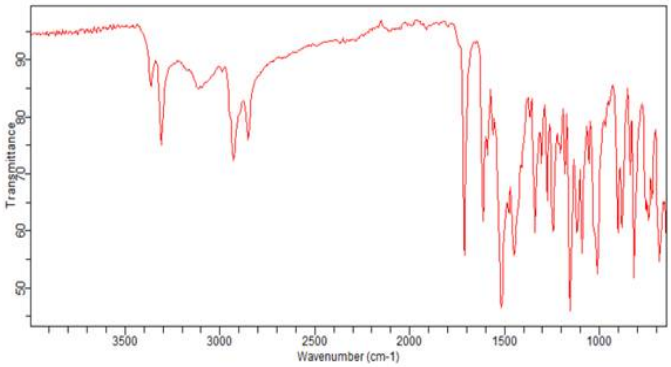

Fig. 8 Glibenclamide + Black Cumin Seeds Chloroform Extract

F8

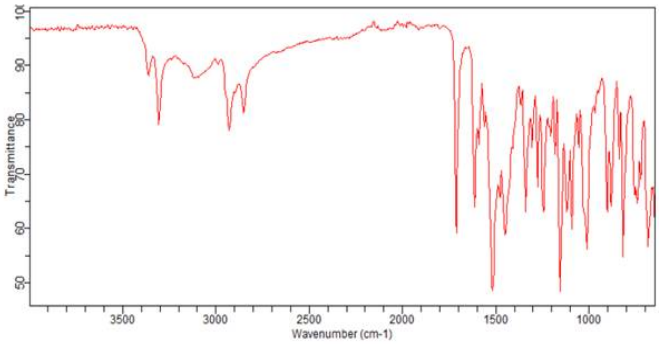

Fig. 9 Glibenclamide + Black Cumin Seeds Butanolic Extract

F9

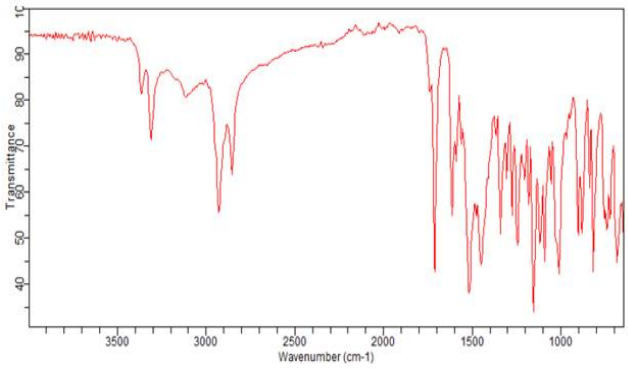

Fig. 10 Glibenclamide + Black Cumin Seeds Methanolic Extract

F10

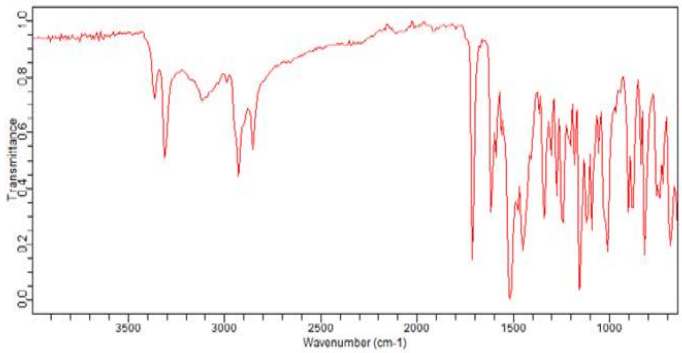

Fig.11 Glibenclamide + Black Cumin Seeds Ethanolic Extract

F11

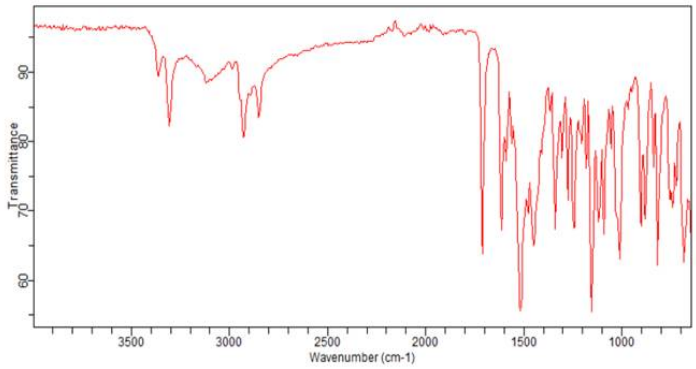

Fig. 12 Glibenclamide + Black Cumin Seeds Aqueous Extract

F49

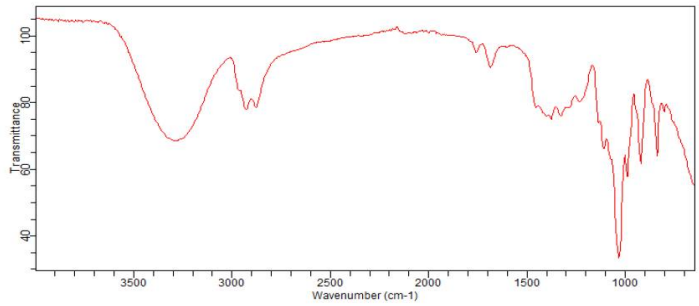

Fig.13 Glibenclamide+polymer

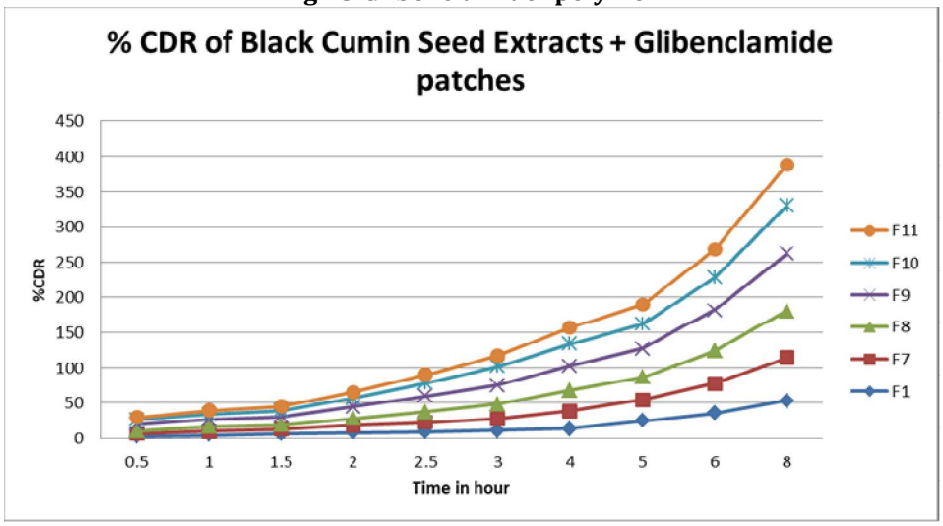

Fig. 14 % CDR of Black Cumin seed Extract and Glibenclamide

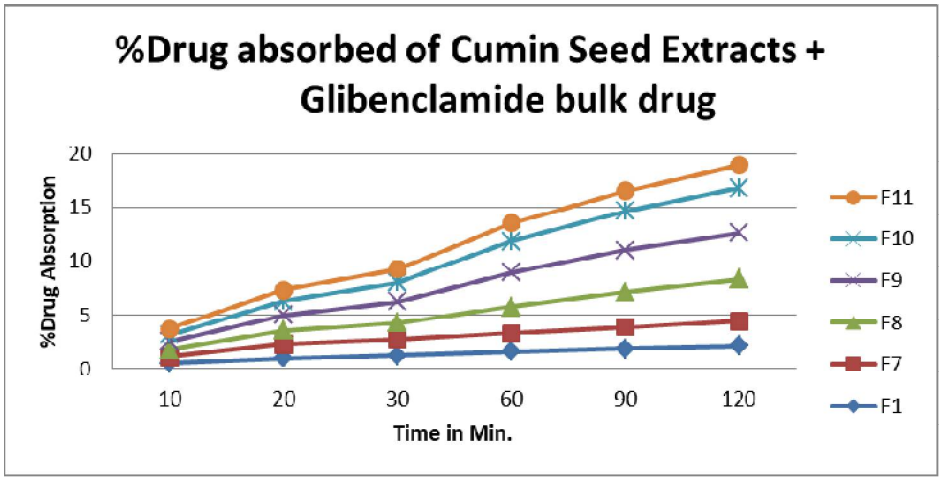

Fig. 15 % Drug Absorption of Black Cumin seed Extract and Glibenclamide

CONCLUSION

It can be concluded that herbal drugs inside the shape of extract can also be used in formulating transdermal patches because of opportunity of launch of drug formula which is very novel approach. The Glibenclamide patches made by way of solvent evaporation approach comprising of various extract of black cumin seed at the side of Glibenclamide had been formulated. The drug became observed likeminded distinctive extracts and the polymers. All extracts indicates to a degree bioenhancing impact compared to person Glibenclamide patch. Among all the formulations f9 shows massive increase in drug release and drug absorption.

ACKNOWLEGEMENT

The authors are very thankful to Leben Laboratories Pvt. Ltd., Akola (MAHARSHTRA) for providing gift samples of Glibenclamide, to conduct this study.

CONFLICT OF INTEREST

Authors have no conflict of interest regarding this research work.

REFERENCES

1. Atal Naveen and Bedi K.L.: Bioenhancers Revolutionary concept to market. J Ayurveda Integr Med. 2010; 1(2): 96–99.
2. Barve Kalyani, Ruparel Kushal: Effect of Bioenhancers on Amoxicillin bioavailability. ADMET & DMPK 2015; 3(1): 45-50.
3. Gupta J., Irchhiaya R., Garud N., Tripathi P., Dubey P., Patel J.: Formulation and evaluation of matrix type transdermal patches of Glibenclamide. International Journal of Pharmaceutical Sciences and Drug Research 2009;1(1):46-50.
4. Bhanja Satyabrata, Singh Rawat, Sudhakar Muvvala, Panigrahi Bhushan,; Design development and evaluation of transdermal patches of Ramipril. International Journal of advances in pharmacy, Biology and chemistry2014;3(2):352-360
5. Agarwal S, Gautam G: Formulation, Development and Evaluation of Atorvastatin Ethosomal Gel. Int. J. Pharm. Investigation 2020;10(4):452-455
6. Ahmed S. Abdul jabbar: In-vitro; ex-vivo assessment of anti-inflammatory Tapentadolloaded non-ionic surfactant vesicular systems for effective transdermal delivery Sys. Rev Pharm 2020;11(12):636-643
7. Singh Amandeep and Bali Alka: Formulation and characterization of transdermal patches for controlled delivery of duloxetine hydrochloride. Journal of Analytical Science and Technology; 2016 7(25): 2-13.
8. Tirunagari Mamatha, Jangala Venkateswara Rao and Nandagopal Anitha: Development and Physicochemical, In Vitro and In Vivo Evaluation of Transdermal Patches of Zaleplon. Indian Journal of Pharmaceutical Education and Research 2013; 47 (4):49-58.
9. Dhanalakshmi1S., Harikrishnan, N. Devi M., Keerthana v., vijayalakshmi: Fabrication and evaluation of herbal transdermal flim from hibiscus rosa sinensis. Int J Curr Pharm 2019; 11(5):101-105.
10. Umekar M.J., Biyani D.M., Amgaonkar Y.M., Bhoyar P.K., Lade U.B. and Kalsait R.P: Formulation Development and Evaluation of Transdermal Drug Delivery System of Antihypertensive Drug. Research Journal of Pharmacy and Technology 2010; 3(3):1-8.

11. Buckley Stephen T., Fischer Sarah M., Fricker Gert , Brandl Martin; In vitro models to evaluate the permeability of poorly soluble drug entities: Challenges and perspectives. European Journal of Pharmaceutical Sciences 2012: 235–250
12. Saha Rajsekhar, Bhupendar Kuldeep : Pharmacognosy and Pharmacology of Nigella Sativa. International Research Journal of Pharmacy 201;2(11):36-39
13. Paliwal Ritu, A. Muhammad and Dahiru Naziru; Phytochemical Analysis, Physichemical Activity and Antibacterial Effects of Cinnamon Zeylanicum, Extract. International journal of engineering sciences & research technology2018; 7(4):162-170.
14. Abdurohaman Mengesha Yessuf; Phytochemical Extraction and Screening of Bio ActiveCompounds from Black Cumin (Nigella Sativa) Seeds. Extract American Journal of Life Sciences2015; 3(5): 358-364.
15. Bharathi P., Swathi1T. , Madhavi1 B., Jasinth1D. ,. Priyanka C, Satya B.Formulation development, in vitro and in vivo evaluation of matrix transdermal systems of Glibenclamide. International Journal of Research in Pharmaceutical and Nano Sciences2013;2(2):242-250.
16. Chavan Sayali, Salunkhe Pranali, Mohite Namrata and Shinde Charushila formulation and evaluation of oral fast dissolving film. International Journal of Current Advanced Research 2019; 8(6A):19028-30.
17. Yadav Pavan Kumar, Mishra Saurabh, Transdermal patch of an antihypertensive drug: its development and evaluation. World Journal of Pharmaceutical Research2017;6(4) : 1355-74.
18. Hanumanaik Mudavath, Patil Umesh, Kumar Gaurav, Patel Sandeep Kumar, Singh Ishwar, Jadatkar Kishor; Design, Evaluation And Recent Trends In Transdermal Drug Delivery System. A Review International Journal of Pharmaceutical Sciences and Research 2012; 3(8):2394-2406.
19. Kriplani1Priyanka, Sharma Abhishek, Aman, Pun Pooja, Chopra Bhawna, Dhingra Ashwani and Deswal1 Geeta; Formulation and Evaluation of Transdermal Patch of Diclofenac Sodium. Global Journal of Pharmacy & Pharmaceutical Sciences 2018; 4(4):1-4.
20. Prabhu Prabhakar, Shah Samip, Gundad Shankar; Formulation development and investigation of domperidone transdermal patches. International Journal of Pharmaceutical Investigation 2011;1(4):240-46.
21. Premjeet Sandhu, Bilandi Ajay, Sahil Kataria and Akanksha Middha; Transdermal Drug Delivery System (Patches), Applications In Present Scenario. International Journal Of Research In Pharmacy And Chemistry 2011; 1(4):1139-51.
22. Raza1Rihan, Mittal1Ashu, Kumari Puspendra, Alam Sanjar, Prakash Surya, Chauhan Nitesh;Approaches and evaluation of Transdermal drug delivery system. Int. J. Drug Dev. & Res. 2015; 7(1):222-233.
23. Idrees Arfat, Rahman Nisar Ur, Javaid Zeeshan, Kashif Muhammad, Aslam Irfan, Abbas Khizar, Hussain Talib; In Vitro Evaluation Of Transdermal Patches Of Flurbiprofen With Ethyl Cellulose. Pharmaceutica Drug Research 2014;71(2):287-295.
24. Shankar S.J., Kapadiya Palak, Prabhu Makaranda, Raju Prathan: Formulation and Evaluation of Transdermal Patches of An Antidiabetic Drug of Glibenclamide. World Journal of Pharmacy and Pharmaceutical Sciences 2015;5(1):522-41.
25. Srilakshmi A., Teja Ravi, Lakshmi K., Thippesh M., Ummehani Sk., Salma,B. :Formulation and evaluation of transdermal patches of Irbesartan. Indian Journal of Research in Pharmacy and Biotechnology 2017;5(3):212-15.
26. Yadav Pawan kumar, Mishra Saurabh: Transdermal patch of an Antihypertensive Drug:it's development and Evaluation. World Journal of Pharmaceutical Research 2017;6(4)1355-74.
27. Jin-Yang Shen,Xiao-Lin Yang, Zhong-Lin Yang Jun-Ping Kou, Fei Li: Enhancement of absorption and bioavailability of echinacoside by verapamil or clove oil. Drug Design, Development and Therapy 2015; 9:4685–93
28. Zhiqiang Luo,Yang Liu, Baosheng Zhao, Mingmin Tang, Honghuan Dong, Lei Zhang,Beiran Lv, Li Wei:Ex vivo and in situ approaches used to study intestinal absorption. Journal of Pharmacological and Toxicological Methods 2013; 68:208–216.

CITATION OF THIS ARTICLE

Ashish Kandalkar, Nitu Singh. Formulation And Development Of Transdermal Patches Of Glibenclamide And Comparative Effect Of Black Cumin Seed Extracts On *Ex Vivo* Release. Bull. Env. Pharmacol. Life Sci., Vol 10[5] April 2021: 146-155.