Research Article **CODEN: AJPAD7** **ISSN: 2321-0923**

Asian Journal of Pharmaceutical Analysis and Medicinal Chemistry

Journal home page: www.ajpamc.com

FTIR SPECTROSCOPIC INVITRO DRUG COMPATIBILITY DETERMINATION OF DICLOFENAC DIETHYLAMINE WITH DIFFERENT SOLVENT SYSTEMS

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ABSTRACT

Diclofenac Diethylamine shows therapeutic value against various disease conditions. The present study is to determine the possibility of developing fingerprint characteristic of diclofenac diethylamine by using different solvent systems such as coconut oil, glycerol, propylene glycol, sesame oil, 2-propanol,benzyl alcohol, chromophore RH 40 for the preparation of topical formulations such as cream, gels etc. identification of functional groups frequencies with the help of fourier transform infrared spectroscopy has been made for the solvent suitability of diclofenac diethylamine with suitable solvent were studied for the topical gel formulation. From FTIR (400 cm^{-1} to 4000 cm^{-1} region) spectroscopic studies were carried out and spectrum were used for identification for invitro drug and solvents compatibility study. Among this study only one solvent not suitable with diclofenac diethylamine such as benzyl alcohol due to the additional peaks observed in the spectrum combination (1871, 1842, and 1811cm^{-1}).

KEYWORDS

Diclofenac diethylamine, Solvents, Topical gel and Compatibility studies.

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INTRODUCTION

Diclofenac diethylamine (DDEA) chemically, *N*-ethylethanamine 2-[(2,6- dichlorophenyl) amino] benzeneacetate was shown in Figure No.1 is a powerful non-steroidal anti-inflammatory drug (NSAIDs)[1], which has been most commonly used to reduce inflammation and local pain[2] associated with muscle or joint injuries such as sprains, strains, or sports injuries. It is used for topical application[3] and mainly used to relieve acute pain. DDEA is a prostaglandin synthetase enzyme inhibitor[4]and has

many advantages such as less adverse reaction, small dose and little individual difference and so on. Gels for dermatological use have several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, nonstaining, compatible with several excipients, and water-soluble or miscible[5].

MATERIALS AND METHODS

Drug sample of Diclofenac diethylamine was kindly supplied by arthi drugs chemicals.

Chemicals used

Coconut oil, sesame oil, Glycerol, 2-propanol, chromaphore RH 40, KBr, Distilled water.

Methods

Perkin Elmer spectrometer Rx (I)

The FTIR imaging in the present investigation was performed using an interfaced with infrared (IR) microscope operated in reflectance mode. The microscope is equipped with a video camera, a liquid nitrogen-cooled mercury cadmin telacid. Detector and a computer controlled translation stage, programmable in the X and Ydirections. Here KBr pellet method was used for sample preparation for FTIR study. The spectra were collected in the 400 cm to 4000cm region with 8cm resolution, 60 scans and beam spot size of 10µm to 100µm the results are below and compared.

Sample preparation

In the present study, IR spectra are to be taken for pure drug, pure solvents and drug solvent solution.

FTIR Spectroscopic analysis for solid samples (Drug sample)

A KBr pellet was prepared by grinding the solid sample with solid potassium bromide (KBr) and applying great pressure to the dry mixture. 2 mg of each drug sample was taken with dry IR grade KBr at about 2 % sample to KBr ratio in a mortar. The grinding was performed until it was uniformly distributed throughout the KBr. Some amount of the mixture was transferred to the pellet making die and by applying as some pressure to the die before pulling the vacuum. Then full pressure of 8000 pounds to 15000 pounds was applied to the die for 2min. Initial vacuum was released along with pressure. Then a vacuum was pulled for 1 to 2 min. The die set was disassembled by removing the base by twisting it off and releasing the U ring. Then the pellet was discharged by using the clear cylindrical pellet extractor located above the end of the bore and the plunger located between the assemblies. Usually the background was first scanned by using a blank potassium bromide pellet. Then the sample was scanned. The spectra was collected in the region of $400cm^{-1}$ to $4000cm^{-1}$ with $8cm^{-1}$ resolution 60 scan and beam spot size of 10 to 100µm.

FTIR Spectroscopic analysis for liquid samples and solution (Pure solvent and Drug + Solvent)

IR spectra of liquid compounds may be obtained either from the pure liquid or from a solution of the liquid in an appropriate solvent. To run a pure liquid, a drop of the liquid is to be placed on the face of a highly polished salt plate (such as Nacl, KBr). Then a second plate is placed on the top of the first plate so as to spread the liquid in a thin layer between the plates. To obtain the spectrum from a solution of the sample, a solution is prepared which is of approximately 0.2 M concentration using an appropriate solvent.

The solution is now spread as a thin film between salt plates. The sample cell is now to be placed in the path of IR beam. After obtaining the spectra, a comparison study is made for spectra of individual drug and pure solvent with that of drug- solvent combination spectra.

RESULTS AND DISCUSSION

The present study is to determine the possibility of developing finger print characteristic of diclofenac diethylamine by using different solvent systems. To determine the solvent suitability of diclofenac diethylamine for the topical formulation. Fourier Transform Infrared Spectroscopy was used. The spectral data analysis for the various Drug-solvent combinations was shown in Table 1-15 and Figure No.2-16.

Based on the interpretation of FTIR spectra of individual combinations, it was found that benzyl alcohol was the only solvent to be incompatible with the drug. The observation of additional peaks in the

spectrum (1871, 1842, 1811cm^{-1}) indicates that there might be any chemical reaction between diclofenac diethylamine and benzyl alcohol.

Table No.1: FTIR Spectral data of Diclofenac diethylamine

Diclofenac Diethylamine		
S.No	**cm^{-1}**	**Possibilities**
1	3221	Due to NH stretching/OH stretching
2	3120	Due to NH stretching/OH stretching
3	3001	CH stretching
4	2823	CH stretching , due to CH2-N
5	2735	NH+ stretching
6	2526	NH+ stretching
7	2295	NH+ stretching
8	2233	NH+ stretching
9	1932	NH+ stretching
10	1631	Week NH δ
11	1346	Aromatic CN stretching
12	1342	Aromatic CN stretching
13	1045	Ortho C-Cl stretching

Table No.2: FTIR Spectral data of 2-Propanol

2-Propanol		
S.No	**cm^{-1}**	**Possibilities**
1	3366.14	OH stretch
2	2014.28	CH stretching
3	1654.62	C-O-H
4	1588.09	C-O-H
5	1457.92	OH bending in plane
6	1147.44	OH bending
7	1084.76	CO bending
8	954.59	CH Out of plane bending

Table No.3: FTIR Spectral data of Diclofenac diethylamine + 2-Propanol

Diclofenac Diethylamine + 2-Propanol		
S.No	**cm^{-1}**	**Possibilities**
1	2860.66	CH stretching
2	2014	CH stretching
3	1944.86	NH+ stretching
4	1654.62	C-O-H
5	1566.88	C-O-H
6	1024.08	Ortho C-Cl stretching
7	947.84	CH Out of plane bending
8	410.66	CH Out of plane bending

Table No.4: FTIR Spectral data of Glycerol

Glycerol		
S.No	**cm^{-1}**	**Possibilities**
1	3370	OH stretch
2	1865.79	C-C-O stretch
3	1654.62	C-C-O stretch
4	1556.27	C-C-O stretch
5	1040.41	CH_2
6	949.77	CH out of plane bending

Table No.5: FTIR Spectral data of Diclofenac diethylamine + Glycerol

Diclofeanc Diethylamine+Glycerol		
S.No	**cm^{-1}**	**Possibilities**
1	2885.95	CH stretching ,due to CH_2-N
2	1865.79	C-C-O st

Table No.6: FTIR Spectral data of Chromopore RH 40

Chromophore RH 40		
S.No	**cm^{-1}**	**Possibilities**
1	3467.74	OH stretch
2	3075.9	CH2 stretch
3	2838.7	CH stretch
4	2351.77	CH stretch
5	1960.29	CH stretch
6	1841.69	CH stretch
7	1730.8	C=C st
8	1682.59	C=C st
9	1639.2	C=C st
10	1556.27	C=C st
11	946.01	CH out of plane bending
12	771.39	CH out of plane bending

Table No.7: FTIR Spectral data of Diclofenac diethylamine + Chromopore RH 40

Diclofenac Dietyhylamine + Chromophore RH 40		
S.No	**cm^{-1}**	**Possibilities**
1	3436.56	OH stretch
2	3093.26	CH_2 stretch
3	2867.02	CH stretch
4	2352.73	CH stretch
5	1959.32	CH stretch
6	1841.69	CH stretch
7	1732.73	C=C st
8	1681.62	C=C st
9	1538.92	C=C st
10	1036.92	Ortho C-Cl stretching
11	761.74	CH out of plane bending
12	550.58	CH out of plane bending

Table No.8: FTIR Spectral data of Propylene glycol

Propylene Glycol		
S.No	**cm^{-1}**	**Possibilities**
1	3353	OH stretch
2	1941	C-C stretch

Table No.9: FTIR Spectral data of Diclofenac diethylamine + Propylene glycol

Diclofeanac Dietylamine + Propylene Glycol		
S.No	**cm^{-1}**	**Possibilities**
1	3362.28	OH stretch
2	1940.04	C-C stretch
3	1654.62	Week NH
4	1538.92	Week NH
5	1376.93	Aromatic CN stretching
6	1177.33	Aromatic CN stretching
7	1044	Ortho C-Cl stretching
8	967.13	CH out of plane bending
9	924.7	CH out of plane bending
10	888.06	CH out of plane bending

Table No.10: FTIR Spectral data of Coconut oil

Coconut oil		
S.No	**cm^{-1}**	**Possibilities**
1	2925.48	CH stretching
2	2352.73	CH stretching
3	1743.33	Stretching absorption due to aldehyde(C=O)
4	1556.27	C=O stretch
5	1465.63	Due to CH_2 group
6	1404.89	Due to CH_3 group
8	1150.12	Stretching due to (C-O) esters
9	793.56	CH out of plane bending
10	722.21	CH out of plane bending

Table No.11: FTIR Spectral data of Diclofenac diethylamine + Coconut oil

Diclofeanc Diethylamine+Coconut oil		
S.No	**cm^{-1}**	**Possibilities**
1	2935.48	CH stretching
2	2352.73	C-C triple bond stretch
3	1741.41	Stretching absorption due to aldehyde(C=O)
4	1556.27	C=C st
5	1465.94	Due to CH_2 group
6	1404.89	Due to CH_3 group

7	1160.94	Stretching due to (C-O) esters
8	800.31	CH out of plane bending
9	722.21	CH out of plane bending
10	523.58	CH out of plane bending
11	459.94	CH out of plane bending

Table No.12: FTIR Spectral data of Sesame oil

Sesame Oil		
S.No	**cm^{-1}**	**Possibilities**
1	2925.48	CH stretch
2	2881.13	CH stretch
3	2854.13	CH stretch
4	2352.73	C-C triple bond stretch
5	1746.23	C=O STRETCH
6	1556.27	C=O STRETCH
7	1458.89	CH_2
8	1407.78	OH δ inplane
9	1162.87	CO stretching
10	793.56	CH out of plane bending
11	723.18	CH out of plane bending
12	418.48	CH out of plane bending

Table No.13: FTIR Spectral data of Diclofenac diethylamine + Sesame oil

Diclofenac Diethylamine+Sesame Oil		
S.No	**cm^{-1}**	**Possibilities**
1	2930	CH stretch
2	2352.73	C-C triple bond stretch
3	1743.33	C=O STRETCH
4	1556.27	C=O STRETCH
5	1464.67	CH_2
6	1407.78	OH in plane
7	1172.51	CO stretching
8	796.46	CH out of plane bending
9	723.18	CH out of plane bending
10	534.19	CH out of plane bending
11	418.48	CH out of plane bending

Table No.14: FTIR Spectral data of Benzyl alcohol

Benzyl alcohol		
S.No	**cm^{-1}**	**Possibilities**
1	3347.82	OH stretch
2	2986.23	CH st
3	2874.38	CH2-O st
4	2351.77	CH2-O st
5	1952.57	c-c-c- st
6	1915.93	c-c-c- st
7	1606.41	Aro C-C st
8	1556.27	Aro C-C st
9	1496.49	Aro C-C st
10	1484.92	Aro C-C st
11	1454.06	OH in-plane
12	1254.47	OH in-plane
13	1208.18	OH in-plane
14	1126.22	Ar CH inplane
15	1079.94	Ar CH inplane
16	1067.41	Ar CH inplane
17	1022	Ar CH inplane
18	936.27	Ar CH out of plane
19	931	Ar CH out of plane
20	912.16	Ar CH out of plane
21	607.14	Ar CH out of plane
22	499.47	Ar CH out of plane
23	481.87	Ar CH out of plane

Table No.15: FTIR Spectral data of Diclofenac diethylamine + Benzyl alcohol

Diclofeanc Diethylamine+Benzyl alcohol		
S.No	**cm^{-1}**	**Possibilities**
1	3243.68	Due to NH stretching/OH stretching
2	2987.2	CH st
3	2875.34	CH_2-O st
4	2294.88	NH+ stretching
5	1952.57	C-C-C- st
6	1915	C-C-C- st
7	1871.58	Additional peak due to c=o st or NH st

8	1842	Additional peak due to c=o st or NH st
9	1811.79	Additional peak due to c=o st or NH st
10	1604.41	Aro C-C st
11	1537.95	Aro C-C st
12	1496	Aro C-C st
13	1484.92	Aro C-C st
15	1258.32	OH in-plane
17	1142.62	Ar CH inplane
18	1004.73	Ar CH inplane
19	934.34	Ar CH out of plane
20	912.16	Ar CH out of plane
21	879.38	Ar CH out of plane
22	697	Ar CH out of plane

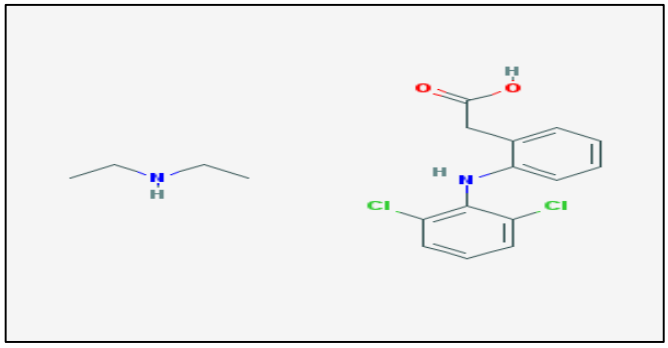

Figure No.1: Diclofenac diethylamine

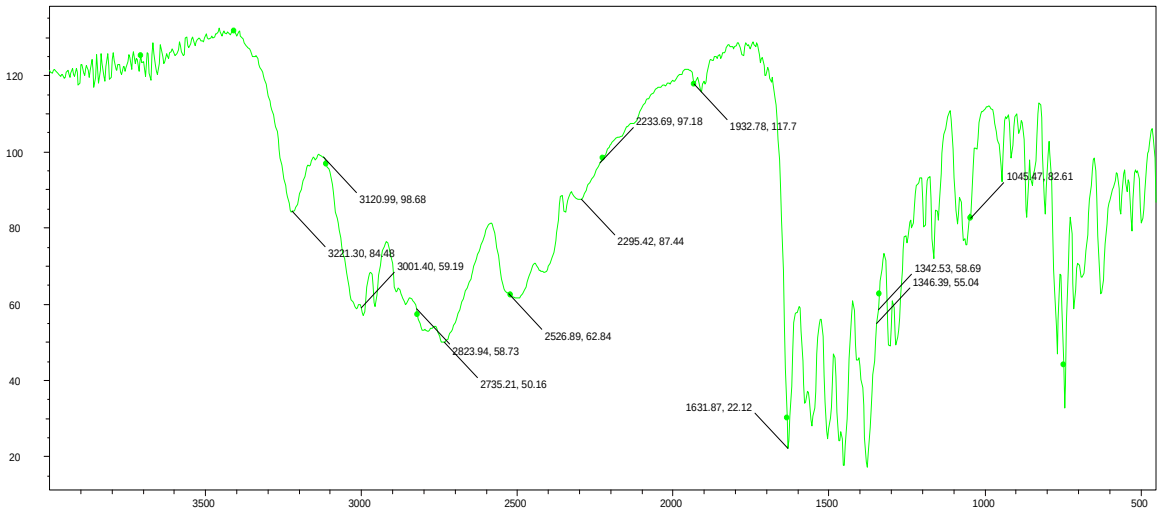

Figure No.2: FTIR Spectrum of Diclofenac diethylamine

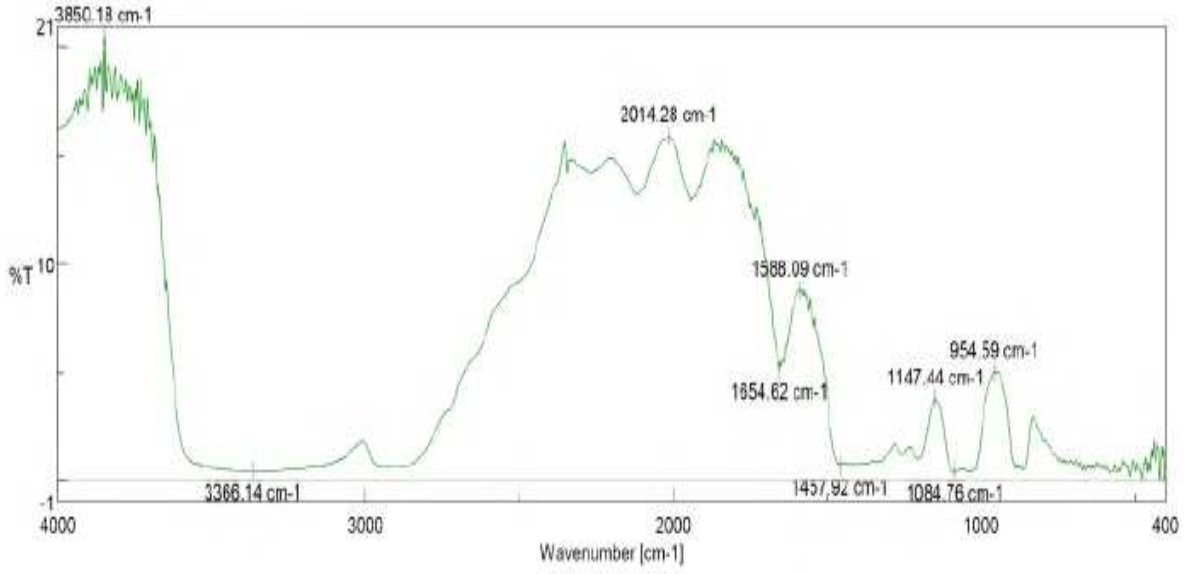

Figure no.3: FTIR Spectrum of 2-Propanol

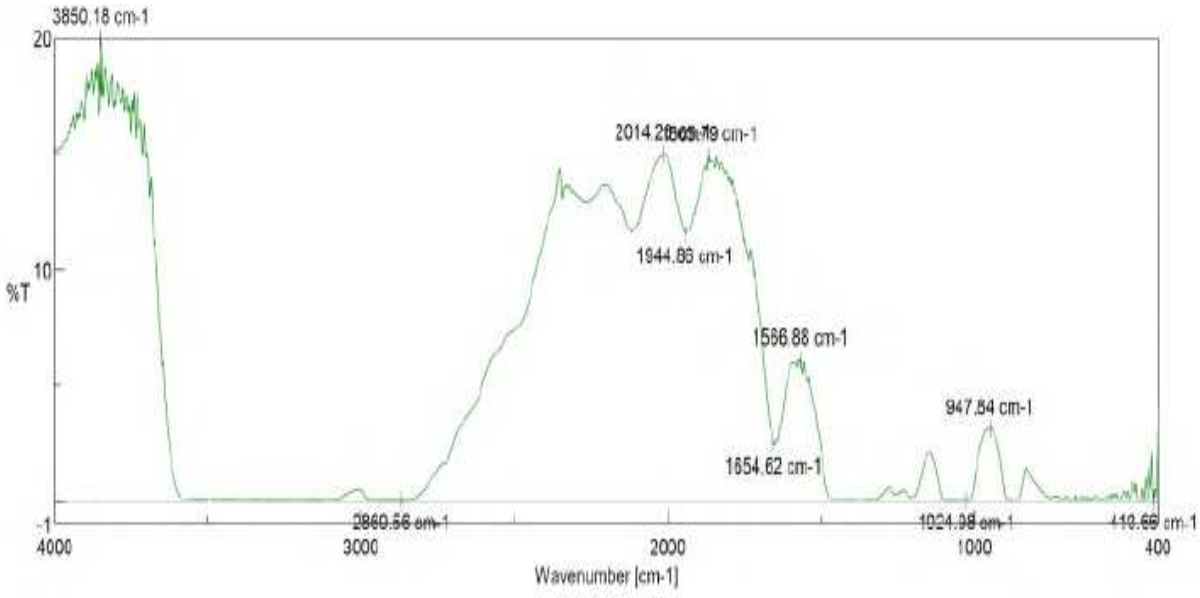

Figure No.4: FTIR Spectrum of Diclofenac diethylamine + 2-Propanol

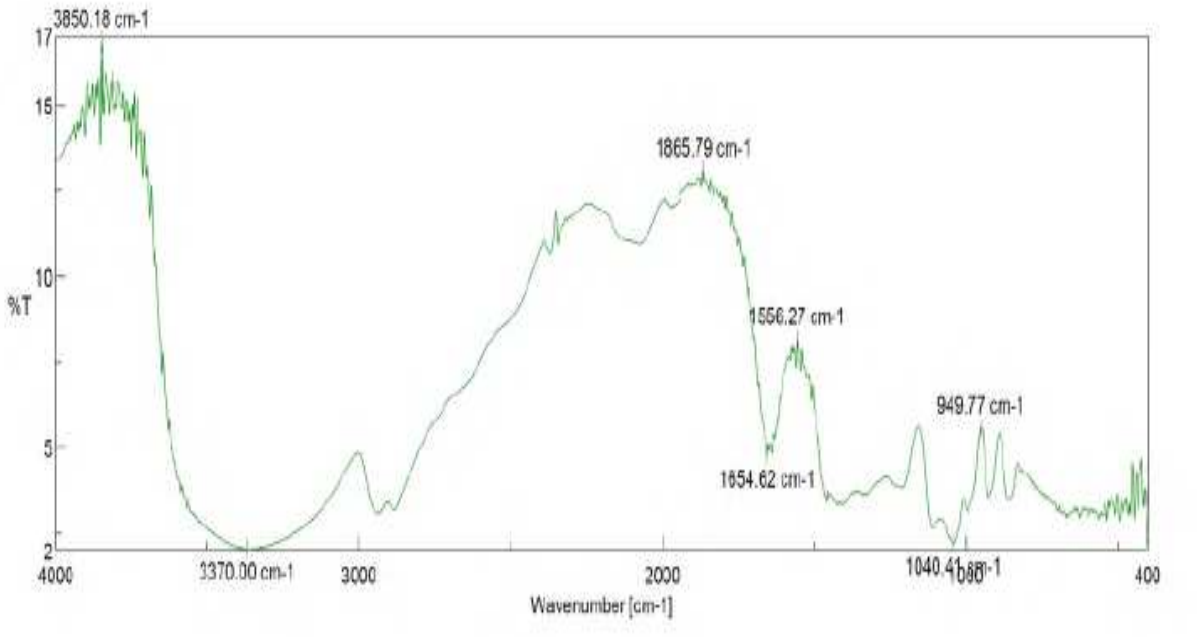

Figure No.5: FTIR Spectrum of Glycerol

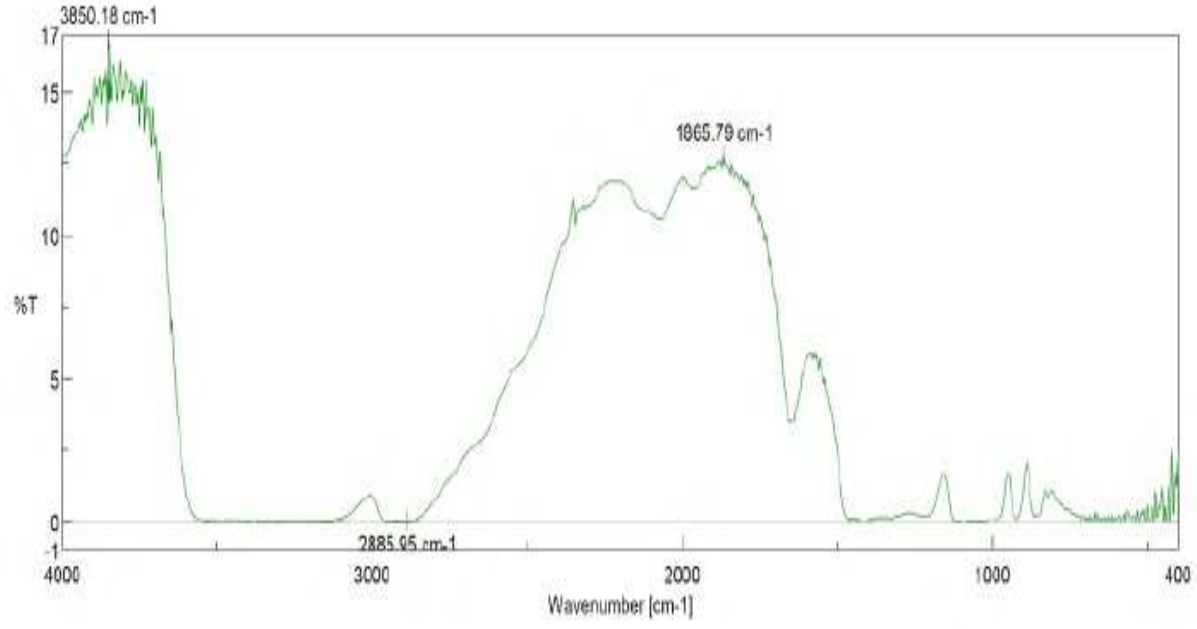

Figure No.6: FTIR Spectrum of Diclofenac diethylamine + Glycerol

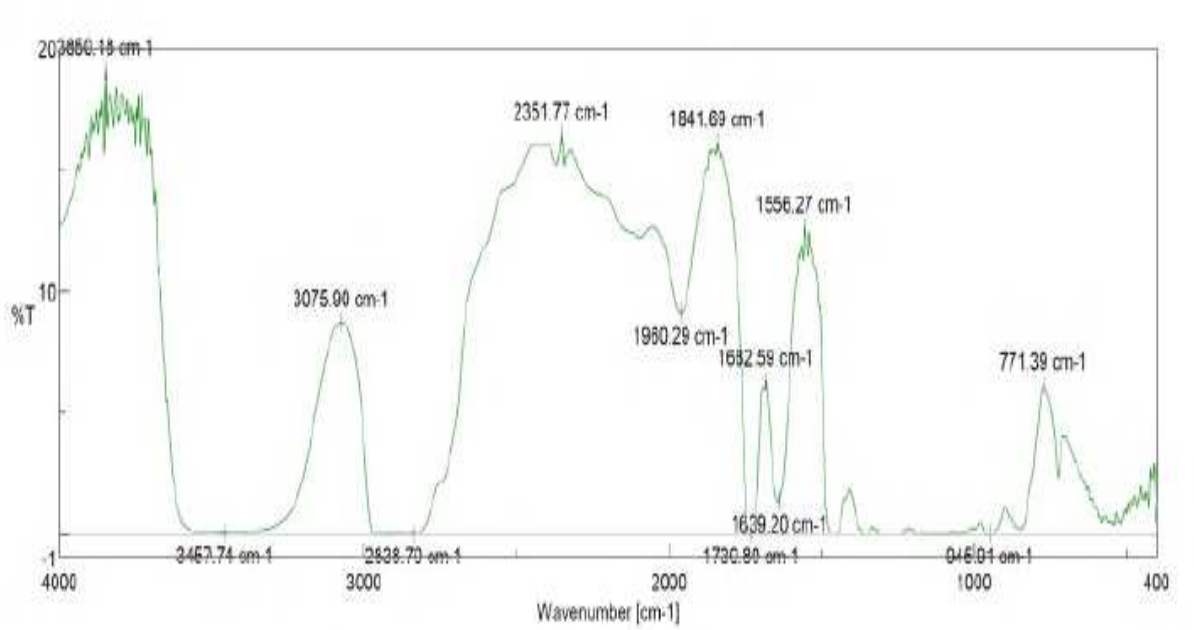

Figure No.7: FTIR Spectrum of Chromopore RH 40

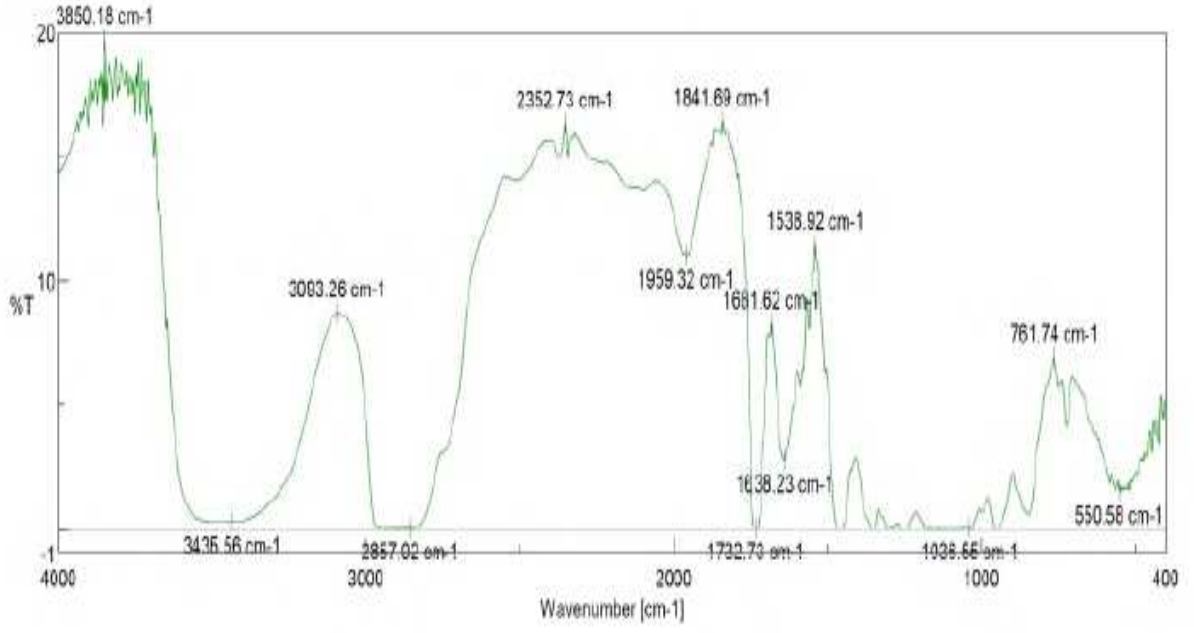

Figure No.8: FTIR Spectrum of Diclofenac diethylamine + Chromopore RH 40

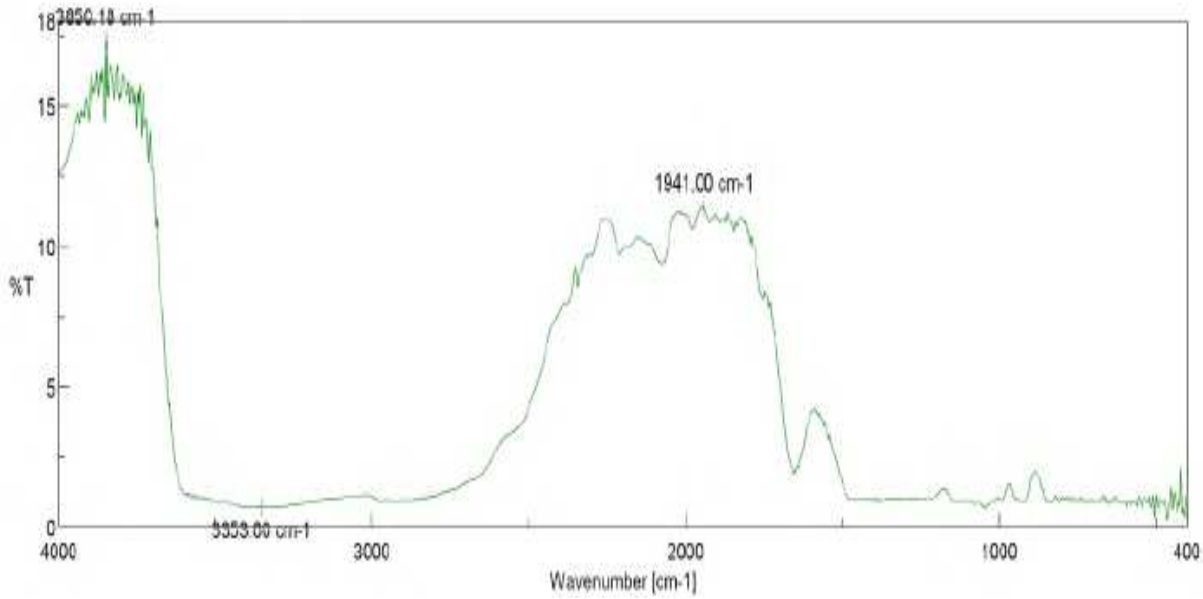

Figure No.9: FTIR Spectrum of Propylene glycol

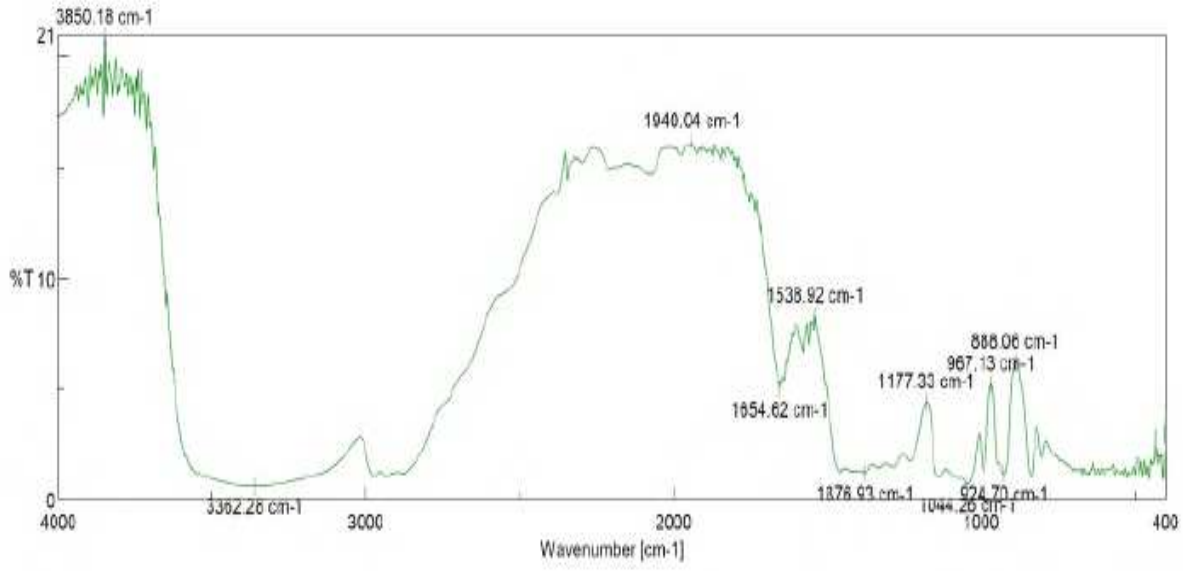

Figure No.10: FTIR Spectrum of Diclofenac diethylamine + Propylene glycol

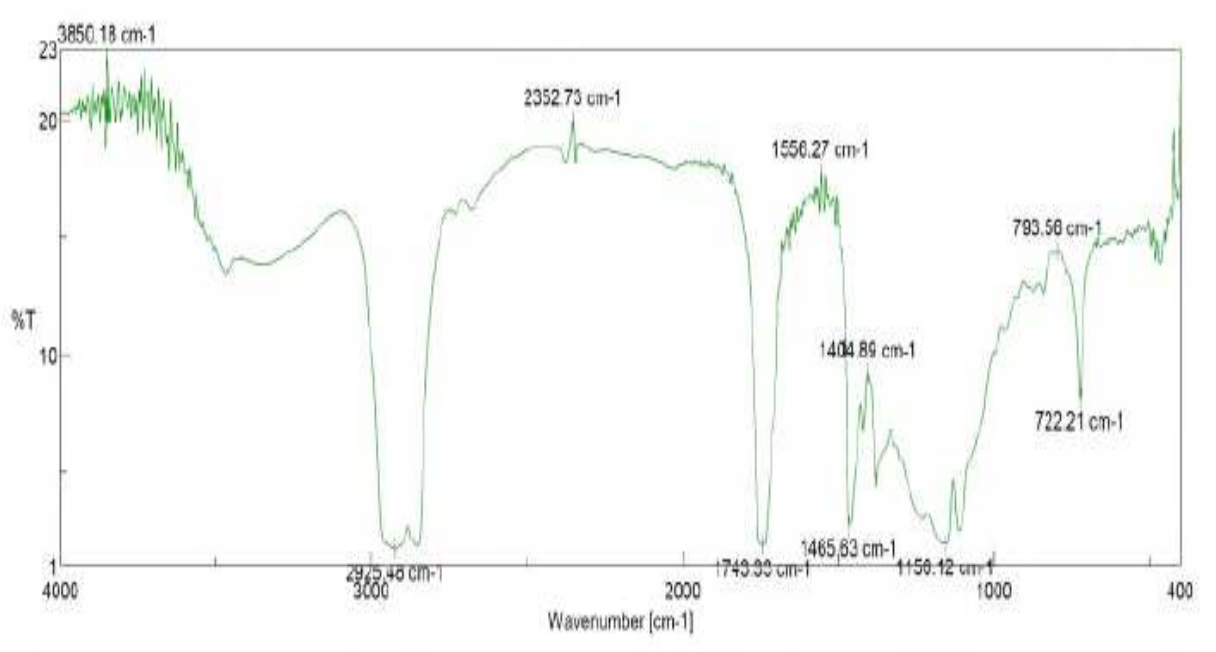

Figure No.11: FTIR Spectrum of Coconut oil

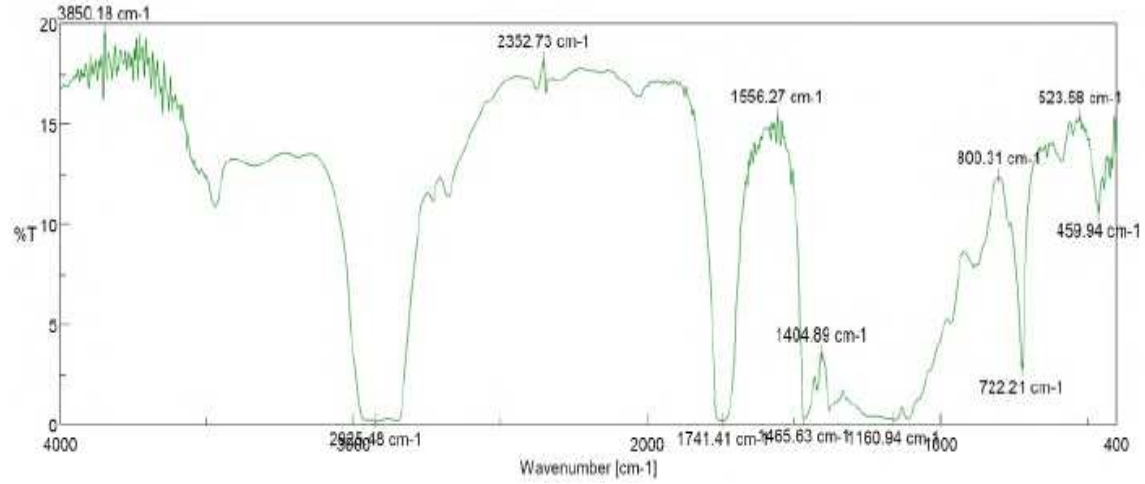

Figure No.12: FTIR Spectrum of Diclofenac diethylamine + Coconut oil

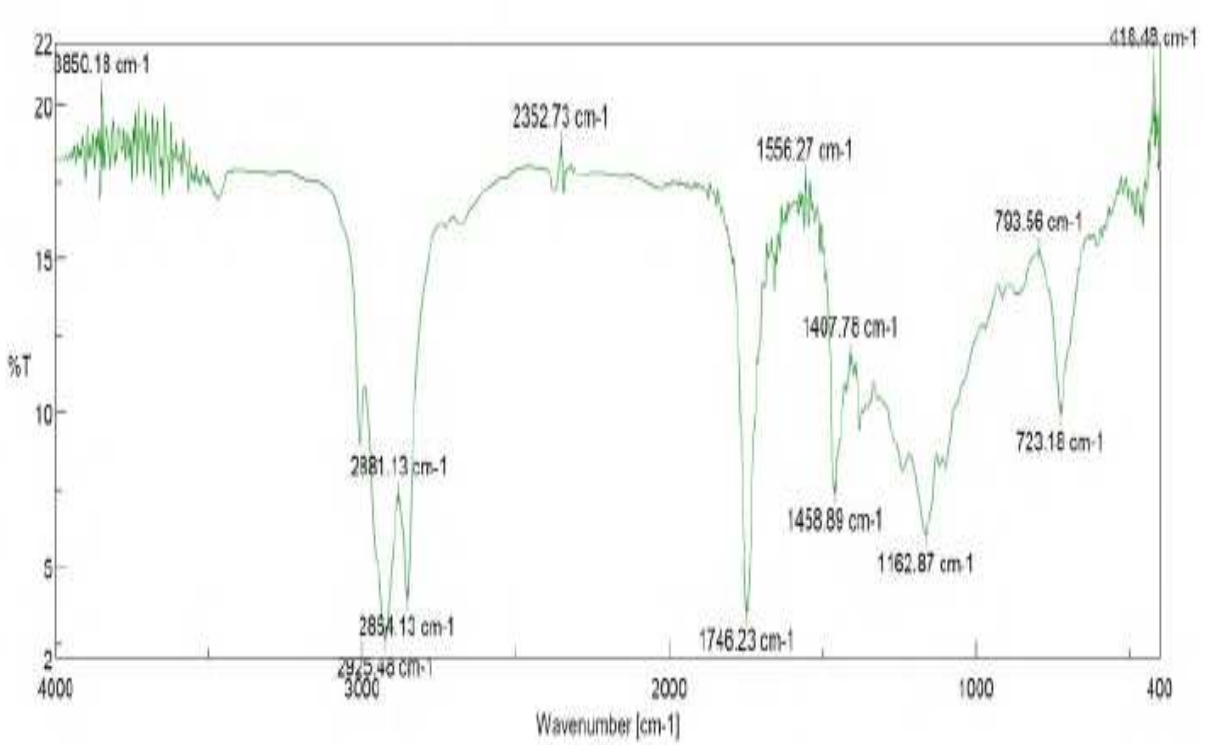

Figure No.13: FTIR Spectrum of Sesame oil

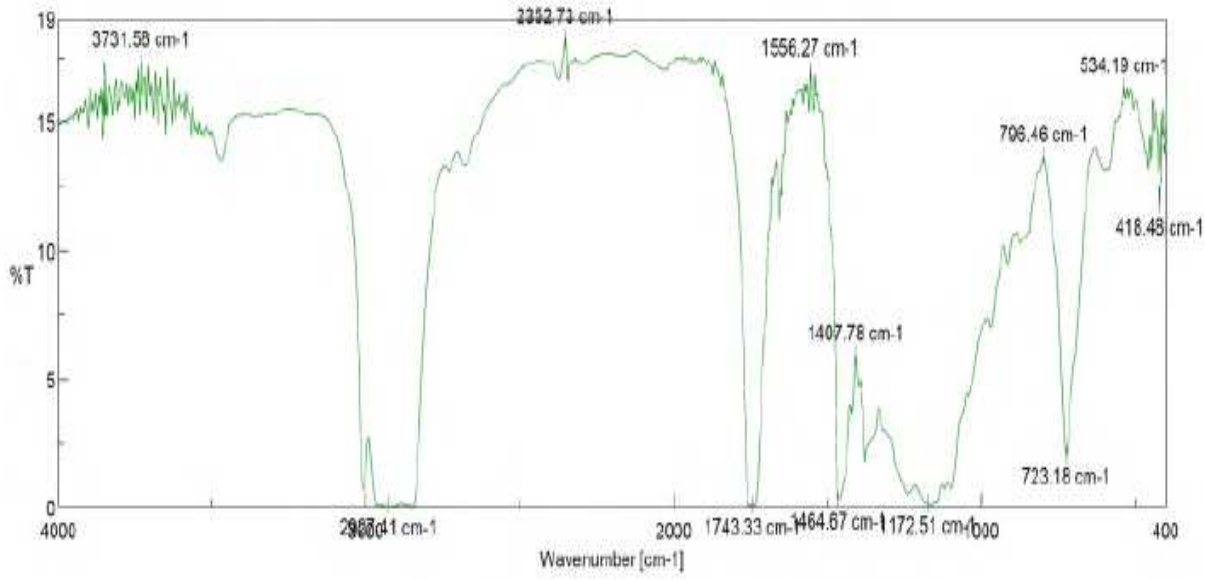

Figure No.14: FTIR Spectrum of Diclofenac diethylamine + Sesame oil

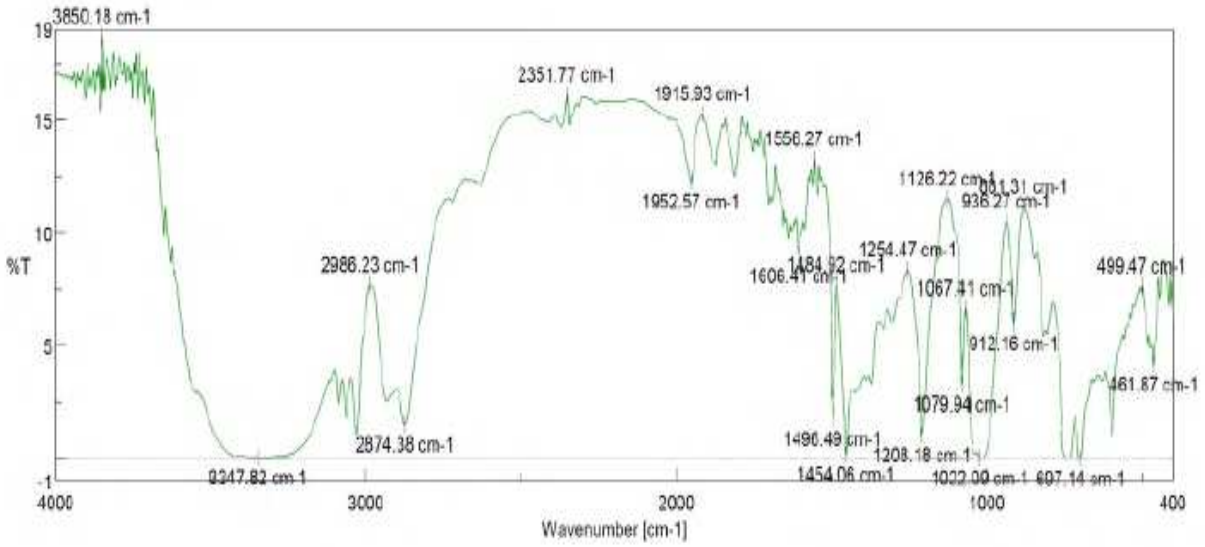

Figure No.15: FTIR Spectrum of Benzyl alcohol

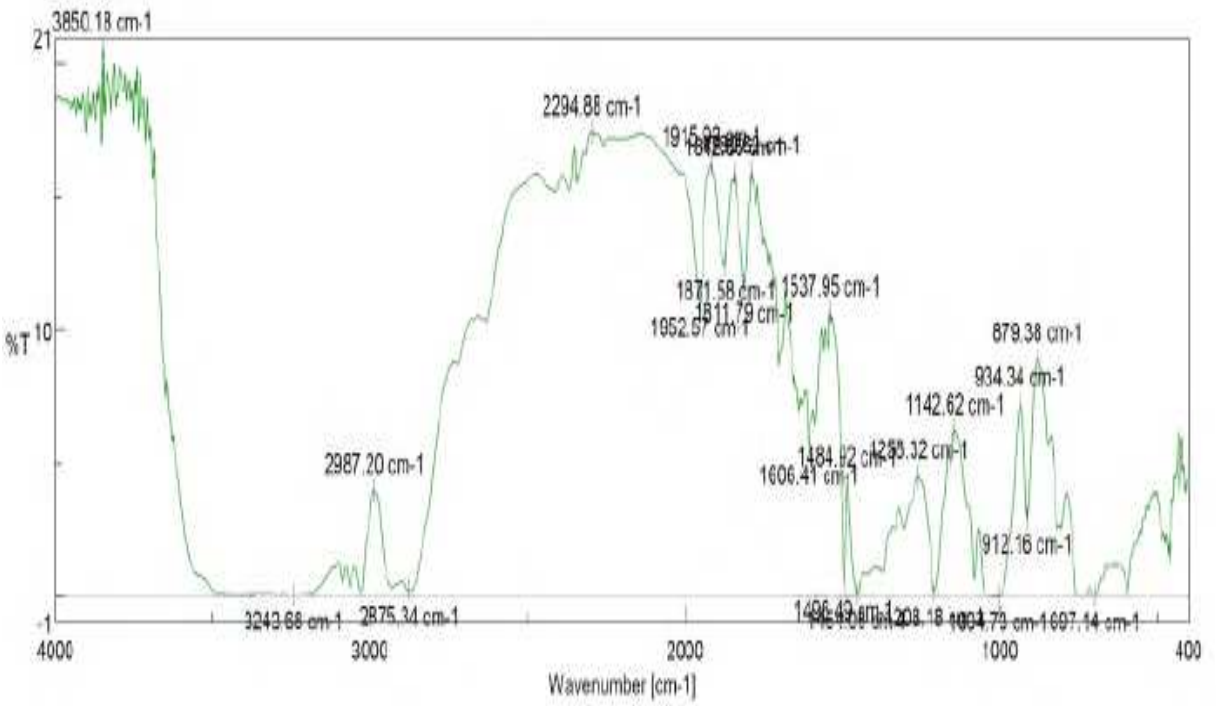

Figure No.16: FTIR Spectrum of Diclofenac diethylamine + Benzyl alcohol

CONCLUSION

From the FTIR spectrum study only one solvent not suitable with diclofenac diethylamine such as benzyl alcohol due to the additional peaks observed in the spectrum combination (1871, 1842, and 1811cm^{-1}). These additional peaks may be due to the possibility of any chemical reactions between diclofenac diethylamine and benzyl alcohol. From that except benzyl alcohol remaining solvents are suitable for the topical dosage formulations of diclofenac diethylamine.

ACKNOWLEDGEMENT

I am thankful to Seven Hills College of Pharmacy, India for providing facility to carry out the research work.

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