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Research Article

Formulation and Evaluation of Niacin extended release Tablets

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ABSTRACT
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Keywords: Niacin, Formulation, Comparative Dissolution, Kinetics, FTIR Spectra.

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CHEMISTRY RESEARCH ARTICLE

Formulation and Evaluation of Niacin extended release Tablets

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ABSTRACT

The objective of the study is to evaluate the release pattern of drug from the fabricated extended release tablets and compare with market sample of the extended release formulation of Niacin tablets over a period of 24 hours. In this paper we are going to discuss graphically such as Stability, Mathematically modeling and drug release kinetic Models such as Korsemeye peppa's Kinetic Model, Higuchi Kinetic Model, First order, Zero order Drug Release, FTIR Spectra, Assay, Comparative Dissolution. It is a potent lipid modifying drug and reduces total mortality, major coronary events, progression of atherosclerosis, coronary artery disease (CAD) mortality, need for revascularization, and incidence of stroke in high risk and CAD patients. Niacin reduces hepatic synthesis of triglycerides (TG) as well as the secretion of very low–density lipoprotein (VLDL) by inhibiting the mobilization of free fatty acids from peripheral tissues. Niacin is the precursor to nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP), which are vital cofactors for dozens of enzymes.

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1. INTRODUCTION

Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration, to obtain rapid and complete systemic drug absorption. Such immediate-release products result in relatively rapid drug absorption and onset of accompanying pharmacodynamics effects. However, after absorption of the drug from the dosage form is complete, plasma drug concentrations decline according to the drug's pharmacokinetic profile. Eventually, plasma drug concentrations fall below the minimum effective plasma concentration (MEC), resulting in loss of therapeutic activity.

An alternative to administering another dose is to use a dosage form that will provide sustained drug release, and therefore maintain plasma drug concentrations, beyond what is typically seen using immediate-release dosage forms. In recent years, various modified-release drug products have been developed to control the release rate of the drug and/or the time for drug release.[1]

A modified release form is defined "as one for which the drug-release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions, ointments or promptly dissolving dosage forms as presently recognized".

Modified drug delivery systems are divided into four categories. [2] Delayed release, extended release, Site specifying targeting and Receptor targeting.

Usually conventional dosage forms produce wide range fluctuation in drug concentration in the blood stream and tissues with consequent undesirable toxicity and poor efficiency. The factors such as repetitive dosing and unpredictable absorption led to the concept of extending drug delivery systems. [3, 4]

The pharmacokinetic profile of niacin is complicated due to extensive first-pass metabolism that is dose-rate specific and, at the doses used to treat dyslipidemia. Multiple daily dosing often is inconvenient for the patient and can result in missed doses, made up doses and patient non-compliance with the therapeutic regimen. When conventional IR dosage forms are taken on schedule and more than once daily, there are sequential therapeutic blood peaks and valleys associated with the taking of each dose i.e., if doses are administered too frequently, minimum toxic concentration (MTC) of drug may be reached with resulting in toxic side effects.

2. DISCUSSION

Calibration curve of the pure drug Niacin was prepared in the concentration range of 5-25 µg/ml at the wavelength of 262 nm. The calibration curve showed good linearity and regression coefficient was 0.999 (R^2).All the tested drug-excipients combinations were not having any effect on the drug and hence, were compatible. Physical mixture of drug and polymer was characterized by FTIR spectral analysis for physical as well as chemical alteration of the drug characteristics. From the results, it was concluded that there was no interference of the functional groups as the principal peaks of the Niacin were unaltered in drug polymer physical mixtures, indicating they were compatible chemically.

Formulation of proper powder blend is the key factor in the production of tablet dosage forms involving extended release of drug from matrix type dosage form. Physical parameters such as specific surface area, shape, hardness, surface characteristics and size can be significantly affect the rate of dissolution of drugs contained in a complex system. The formulated powder blends of different formulations were evaluated for angle of repose, true density, bulk density, compressibility index and Hauser ratio. The results of angle of repose (<30) indicated well to fair flow properties of all the formulated powder blends. The compressibility index value were recorded 16 to 28, result in good flow properties in all formulation. The Hauser ratio value recorded 1.20 to 1.38, result in good to moderate flow of all the formulated powder blends. All these results indicate that the formulated powder blends processed satisfactory flow properties and compressibility.

3. CONCULSION

Formulation and Evaluation of Niacin Extended Release Tablets was undertaken. The study was undertaken with an aim to formulate Niacin as extended release tablets. The literature review showed that Niacin is selective antihyperlipidemic agent improves HDL tolerance in patients with hypercholesterolemia, lowering both LDL, VLDL in plasma lipids. In this efforts were directed towards the formulation development of the rate controlled dosage form for the antihyperlipidemic drug Niacin. During this phase of investigation various factors that likely to affect the performance of the extended release was studied. The release kinetics, dissolution rate, process variables such as hardness, weight variation during granulation are the same factors found critical during the development based on the experimental finding.

Wet granulation method was formulation. Granules were evaluated for tests such as bulk density, Tapped density, Compressibility Index

and Hausner ratio before being punched as tablets. Tablets were tested for weight variation, thickness and friability, in-vitro dissolution tests were performed and percentage drug release was calculated. Dissolution tests were performed and percentage drug release was calculated. In the dissolution modeling all the developed formulations followed Korsemeyer-peppas drug release.

4. EXPERIMENTAL RESULTS

In order to achieve required extended release profile, tablets were prepared by wet granulation technique using different formulations (F-1 toF-11) with different amount of Methocel K4M CR. Criteria for selecting the most appropriate model were based on linearity and diffusion exponent of the respective kinetic model. Drug release mechanism was found as a complex mixture of diffusion, swelling and erosion. The experimental formulation compared well with commercial products and met the proposed standards for controlled-release products. The tablets were evaluated for post-compression parameters like average weight, thickness, hardness, friability, swelling index, floating lag time and total floating time, and *in vitro* drug release studies. In contrast, the press-coated tablets showed a slower dissolution rate compared with simple matrix tablets and the release curve was nearly linear. Dissolution data were fitted to zero order, first order and Higuchi's release kinetics to evaluate kinetic data.

Table No: 1 materials used in matrix tablet formulations

S.NO	Matrix characteristics	Materials
1	Insoluble, Inert	Polyethylene, Polyvinyl chloride, Methyl acrylate-Methacrylate Co-Polymer, Ethyl cellulose
2	Insoluble, Erodible	Carnauba, Steraryl alcohol, Stearic acid, PEG
3	Hydrophilic	Methyl Cellulose, HEC, HPMC, Sodium CMC.

Table No: 2 details of innovator's product [37, 38]

Average weight	1299±5mg
Hardness	25.1Kp
Thickness	8.11±0.2mm
Friability	0.14%

Table No: 3 mathematically modeling and drug release kinetics

Drug release kinetics (R^2)					
Formulations	Zero order	First order	Higuchi	Korsemeyer	**Release exponent (n)**
F1	0.898	0.964	0.996	0.997	0.462
F2	0.919	0.968	0.978	0.995	0.456
F3	0.929	0.904	0.981	0.994	0.471
F4	0.868	0.989	0.990	0.991	0.482
F5	0.873	0.973	0.992	0.994	0.478
F6	0.876	0.964	0.993	0.995	0.480
F7	0.915	0.919	0.994	0.996	0.563
F11	0.950	0.876	0.993	0.996	0.561
F11A	0.988	0.986	0.903	0.992	0.514
F11B	0.926	0.994	0.993	0.995	0.618
F11C	0.888	0.881	0.955	0.958	0.707
F11D	0.966	0.845	0.985	0.997	0.652
F11E	0.971	0.832	0.978	0.997	0.759
Innovator	0.978	0.828	0.974	0.995	0.762

Table No: 4 Stability data of optimized formulation of Niacin extended release tablets.

S.No	Time points (hrs)	Initial	Cumulative % Drug Release (mean ± SD) (n=3)			
			25⁰C/60%RH		40⁰C/75%RH	
			1st Month	2nd Month	1st Month	2nd Month
1	1	9.40 ± 1.20	9.3 ± 1.11	9.28 ± 0.98	9.21 ± 0.33	9.01 ± 0.61
2	3	22.3 ± 0.09	21.6 ± 1.44	20.6 ± 1.44	21.1 ± 1.03	19.4 ± 0.52
3	6	37.1 ± 0.71	35.9 ± 0.47	34.1 ± 0.98	35.1 ± 1.29	34.3 ± 1.13
4	9	50.9 ± 1.16	49.8 ± 1.14	47.2 ± 1.08	49.2 ± 0.99	48.1 ± 1.11

5	12	64.9 ± 0.96	62.7 ± 0.96	61.2 ± 0.31	61.4 ± 1.54	60.3 ± 0.96
6	15	74.5 ± 1.61	73.2 ± 1.23	72.4 ± 0.88	72.1 ± 0.43	71.2 ± 0.83
7	20	87.1 ± 0.53	85.9 ± 1.67	84.5 ± 0.66	85.2 ± 0.76	84.1 ± 0.51
8	24	98.9 ± 0.67	97.6 ± 0.43	96.3 ± 0.98	97.1 ± 0.36	96.2 ± 1.87
9	Assay	100.12 ± 0.2	100.01 ± 1.06	99.95 ± 0.56	99.89 ±0.19	99.37 ±0.31

Table No: 5 Drug-Excipient Compatiblity Spectral study (FTIR)

Drug/ Excipient	Important IR spectral peaks of different groups expressed in cm^{-1}			
	O-H (3800-2700)	**C=O (1850-1650)**	**Aromatic CH (3080-3010)**	**CH Out of Plane (748-704)**
Drug	3445.98	1704.18	3070.81	747.45
Drug + Avicel	3451.76	1704.18	3070.81	747.45
Drug+CollodialSilicondioxide	3423.8	1707.08	3075.63	747.45
Drug + Acetone	3448.87	1707.08	3074.66	747.45
Drug+IsopropylAlcohol	3445.98	1704.18	3072.74	746.48
Drug + Povidone K-90	3445.01	1707.08	3071.77	746.48
Drug + Surelease	3449.84	1705.15	3076.59	748.41
Drug + Mg.Stearate	3428.62	1797.73	3072.74	748.41
Drug+EudragitRL30D	3450.80	1701.29	3072.74	746.48
Drug+EudragitRSPO	3435.37	1706.11	3073.70	748.48
Drug+EudragitRS100	3433.44	1760.12	3070.18	745.52
Drug + Eudragit RL 100	3445.01	1719.61	3072.45	749.38
Drug+DicalciumPhosphatedihydrate	3446.94	1704.23	3073.70	751.31
Drug + Kollicoat SR 30D	3448.87	1706.11	3072.74	748.48
Drug + Povidone K-30	3449.84	1648.24	3076.27	746.48

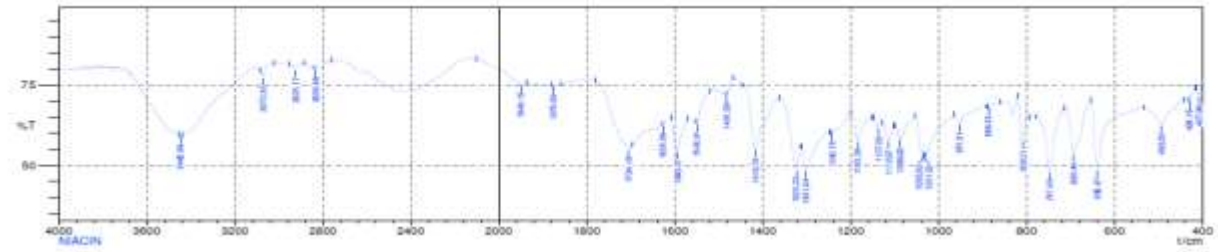

Fig No: 1 FTIR Spectra of Niacin (Drug)

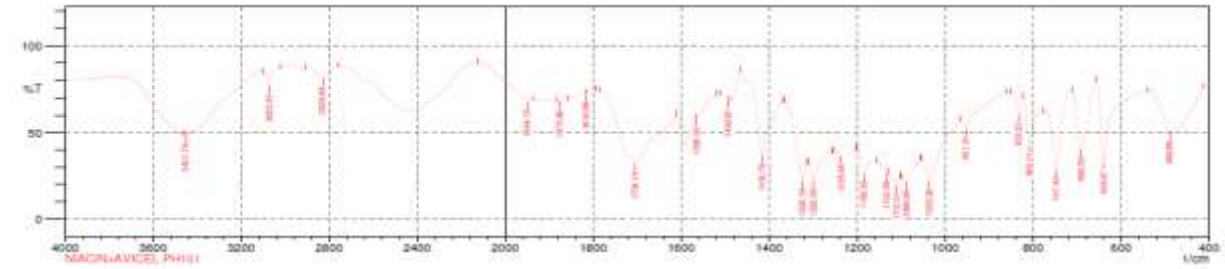

Fig No:2 FTIR Spectra of Drug + Avicel PH 101

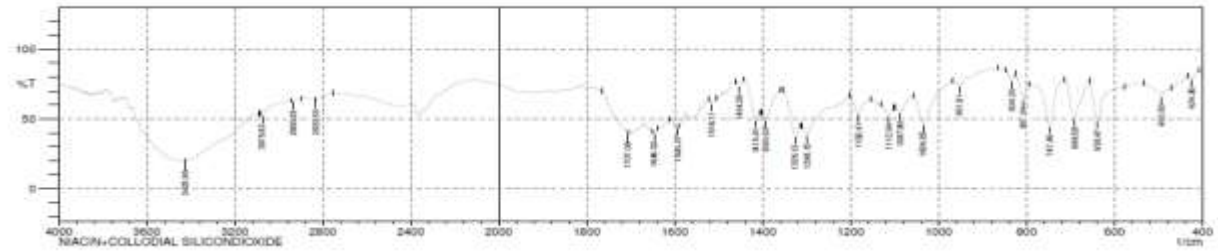

Fig No3 FTIR Spectra of Drug + Collodial Silicon dioxide

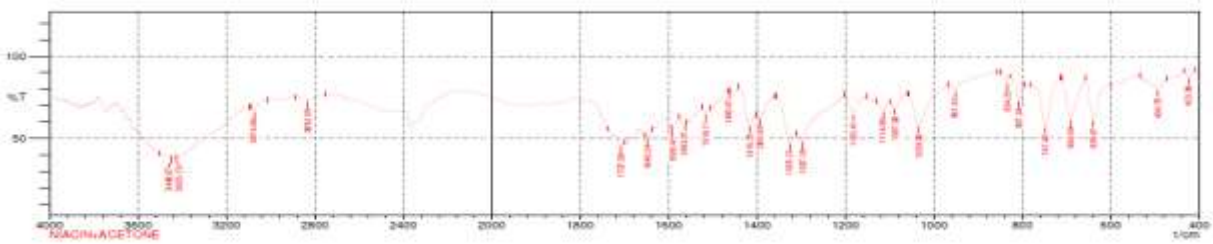

Fig No: 4 FTIR Spectra of Drug + Acetone

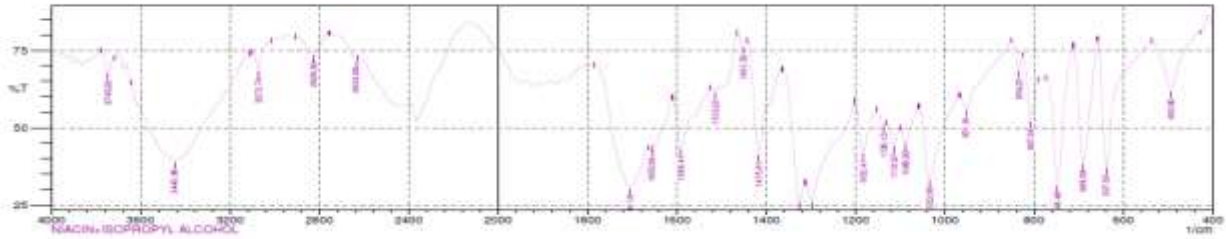

Fig No:5 FTIR Spectra of Drug + Isopropyl alcohol

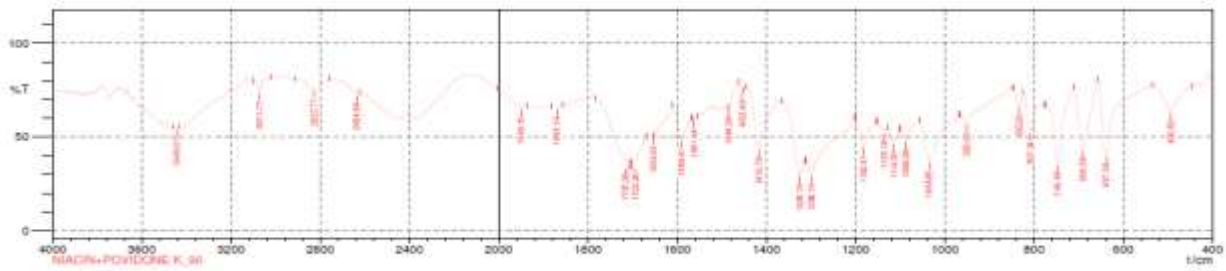

Fig No: 6 FTIR Spectra of Drug + Povidone K-90

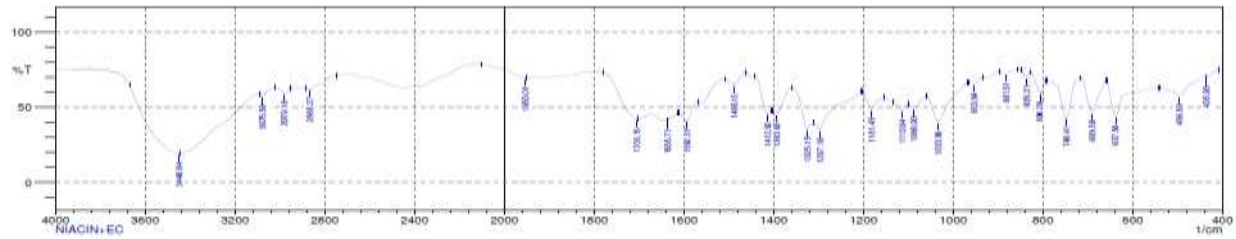

Fig No: 7 FTIR Spectra of Drug + Surelease (Ethyl Cellulose)

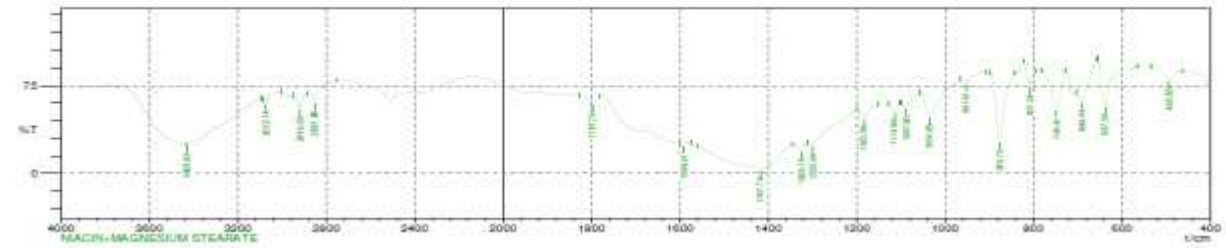

Fig No: 8 FTIR Spectra of Drug + Magnesium Stearate

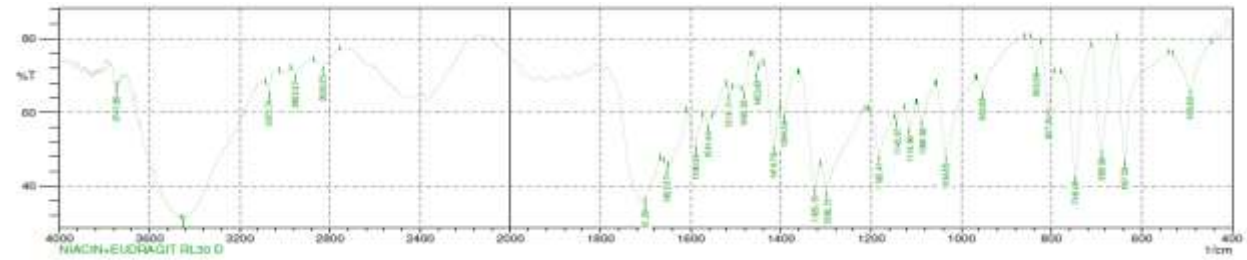

Fig No: 9 FTIR Spectra of Drug + Eudragit RL 30 D

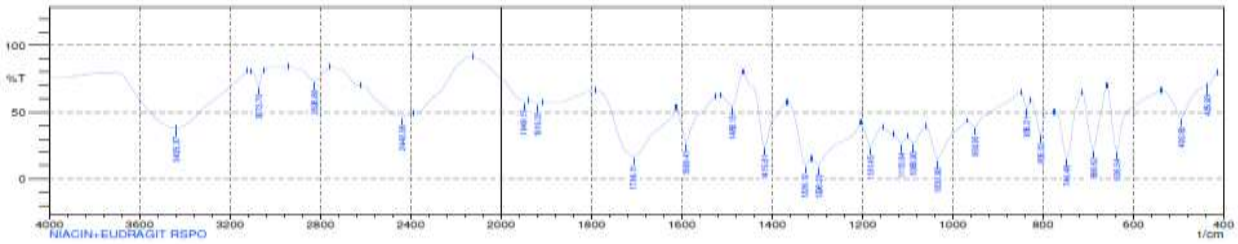

Fig No: 10 FTIR Spectra of Drug + Eudragit SPO

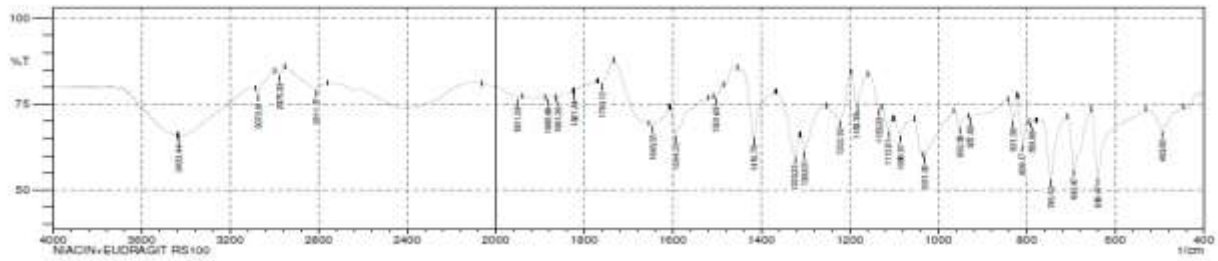

Fig No: 11 FTIR Spectra of Drug + Eudragit RS100

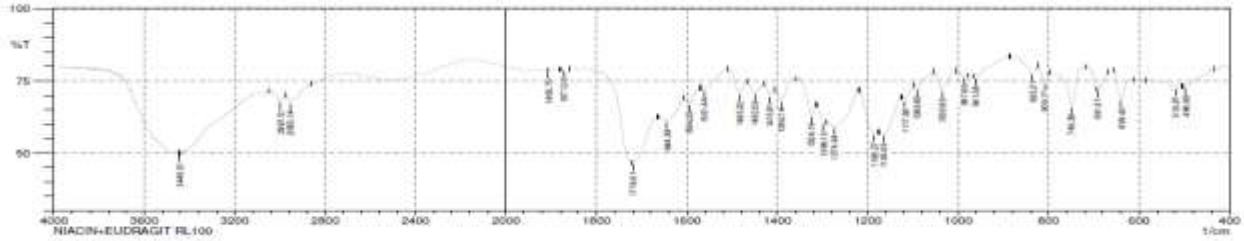

Fig No: 12 FTIR Spectra of Drug + Eudragit RL100

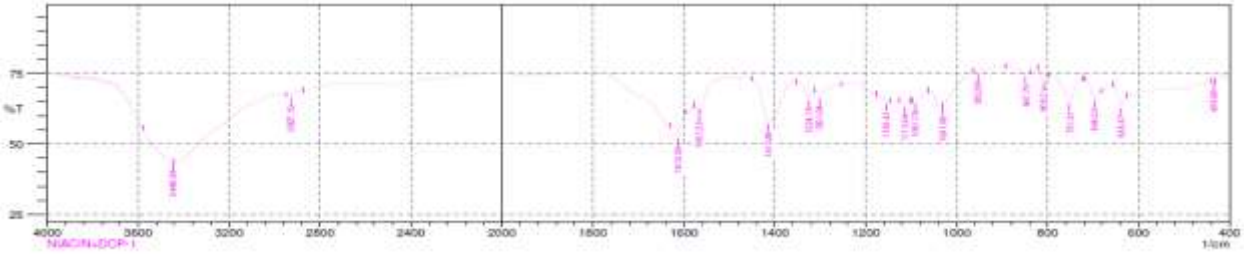

Fig No13 FTIR Spectra of Drug + Dicalcium Phosphate dihydrate

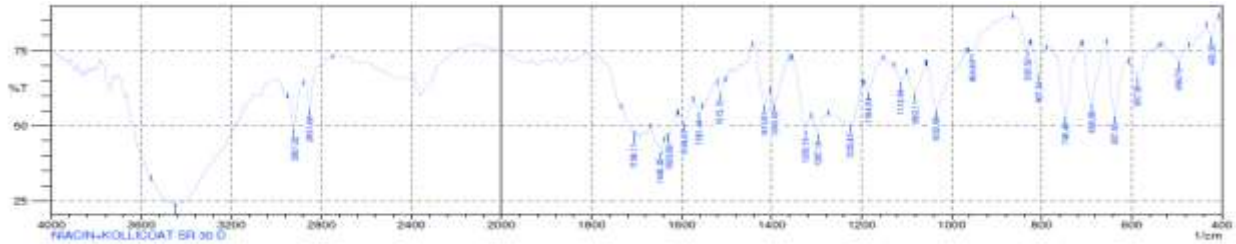

Fig No:14 FTIR Spectra of Drug + Kollicoat SR 30D

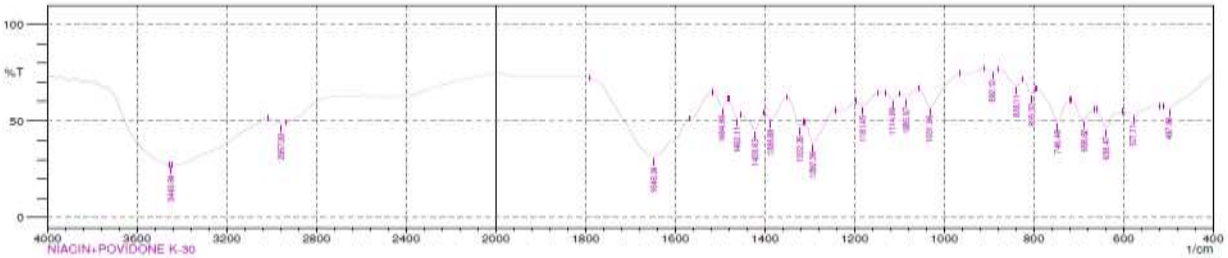

Fig No: 15 FTIR Spectra of Drug + Povidone K 30

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