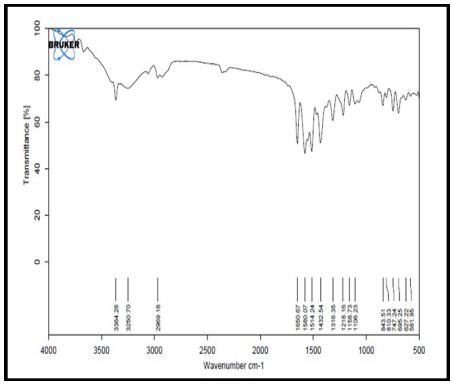
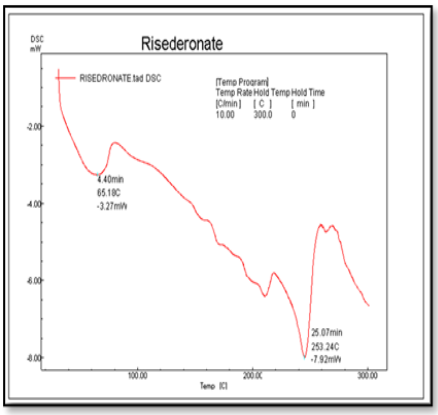
Authentication of drugs

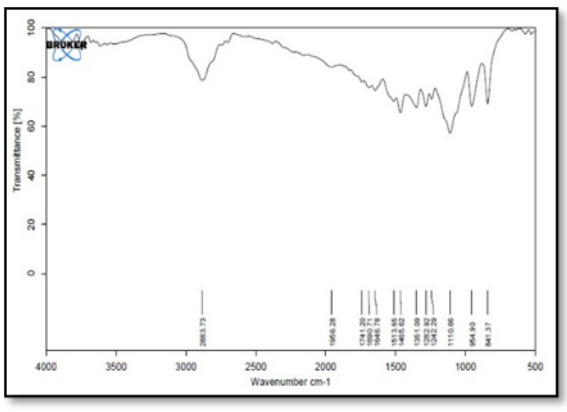


Chapter-4

Preformulation study



Drug-excipient compatibility study



4.1. Preformulation study:

An essential step in the development of novel drug delivery systems is the preformulation study, which focuses on providing the framework for the drug or drug combination with other pharmaceutical excipients in the formulation of the dosage form. Preformulation studies were conducted to gather all relevant information, such as the physical, chemical, mechanical, and biological characteristics of the drug in regard to other ingredients that may have an impact on the formulation design of the drug delivery [1].

4.1.1. Authentication of drugs:

Authentication of drugs (ATO and RSNa) was carried out by organoleptic characteristics, Melting point determination, λ_{max} determination, Fourier Transformed Infrared (FTIR) analysis and Differential scanning calorimetry (DSC).

4.1.1.1. Organoleptic properties of drugs:

The organoleptic characteristics of drugs like color, physical state, and appearance were observed.

4.1.1.2. Melting point determination:

The melting point determination of drugs (ATO and RSNa) was carried out by capillary method. In this method, the capillary was filled with drug and the tube was placed in an electrically operated melting point apparatus (Veego Instrument, India) in which temperature increases gradually. The temperature range at which compound starts melting to completely melted was recorded [2].

4.1.1.3. Differential Scanning Calorimeter (DSC) analysis:

DSC analysis was carried out using a Differential Scanning Calorimeter (DSC-60, Shimadzu, Japan). The samples were scanned in sealed aluminium pan at a heating rate of 10°C per minute in the range of 30 to 300°C under inert nitrogen atmosphere at a flow rate of 40 ml/min [3].

4.1.1.4. Fourier transform infrared (FTIR) analysis:

The infrared absorption spectra of drugs (ATO and RSNa) were measured by FTIR instruments (IR Affinity – 1S, Shimadzu, Japan) using a potassium bromide (KBr)

disk in range of 400-4000 cm^{-1} using resolution of 4 cm^{-1} in an inert atmosphere. Samples were mixed with dry KBr (1:100 ratio) and then compressed into discs under pressure of 600 to 1000 bar [4].

4.1.1.5. Determination of λ_{max} by UV-Vis Spectrophotometer:

a. For Atorvastatin:

Weighed accurately about 10 mg of drug in 100 ml of methanol to make 100 ppm of stock solution. Then aliquot of sample was pipetted out from stock to prepare 10 ppm of sample and made volume upto 10 ml by methanol. The spectrum was recorded against blank.

b. For Risedronate:

Weighed accurately about 10 mg of drug in 100 ml of double distilled water to make 100 ppm of stock solution. Then aliquot of sample was pipetted out from stock to prepare 10 ppm of sample and made volume upto 10 ml by double distilled water. The spectrum was recorded against blank.

4.2. Drug-excipients compatibility study:

The drug excipient compatibility study was performed by FTIR. The drug-excipient mixture was grounded into fine powder and mixed thoroughly with KBr. The samples were prepared by putting 10-12 mTons of pressure in a motorised pellet press. Subsequently, these pellets were scanned in the range of 4000-100 cm^{-1} and spectrum were recorded by using FTIR spectrophotometer (IR Affinity – 1S, Shimadzu, Japan). For the compatibility study, a blend of an equivalent ratio for respective drugs (ATO and RSNa) with excipients (used in formulation) was prepared and analyzed.

4.3. Results and discussion:

4.3.1. Organoleptic characteristics:

The organoleptic characteristics of Atorvastatin and Risedronate are shown in table-4.1.

Table- 4.1. Organoleptic characteristics of drugs

Organoleptic characteristics	Properties	
	ATO	**RSNa**
Physical state	Solid	Solid
Appearance	Crystalline powder	Crystalline powder
Color	White	White

4.3.2. Melting point determination:

The melting point of ATO was found to be 160 to 163 ℃ and it was similar to reported melting point 159-161 ℃ [5]. The melting point of RSNa was found to be 253 to 255 ℃ and it was like reported melting point 252-262 ℃ [6].

4.3.3. FTIR analysis:

The FTIR spectrum of ATO and RSNa is shown in figure-4.1 and figure-4.2 respectively. The data of characteristics peaks is shown in table-4.2 and table-4.3 for ATO and RSNa respectively. The obtained data from spectra were compared with FTIR spectra of respective standard drug and it was found to have similar characteristic peaks, authenticating the drugs.

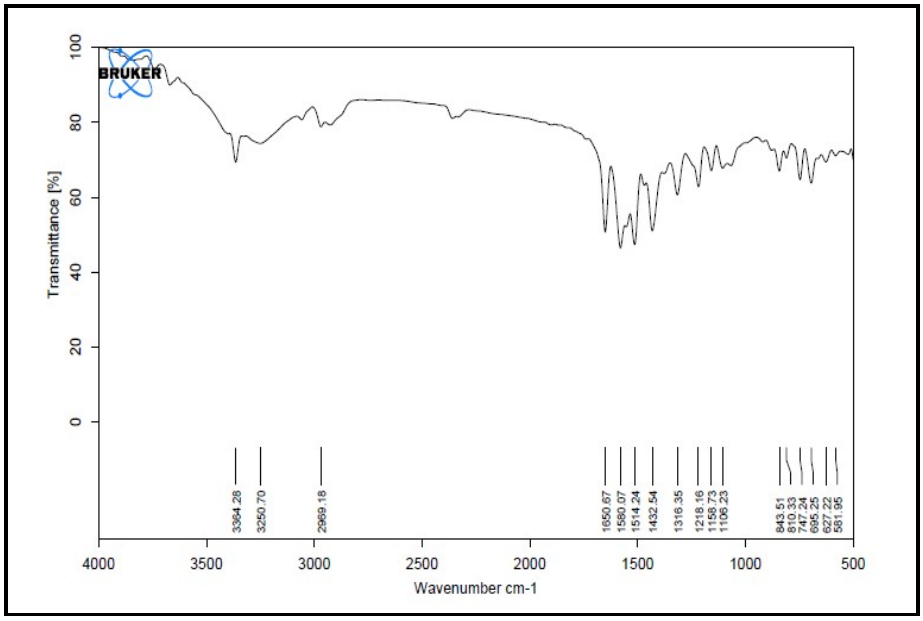


Figure-4.1. FTIR spectrum of ATO

Table-4.2. Characteristic peaks of ATO in FTIR spectrum

Functional Groups	**Reported Range (cm^{-1})**	**Observed Value (cm^{-1})**
Pyrrole (Ring stretching)	1390-1440	1435.04
	1490-1585	1523.76
Carboxylic acid (-OH and -CO combination band)	1390-1455	1435.04
Monosubstituted benzene (-CH out of plane bending)	700-785	746.55
Monosubstituted benzene (-CH stretching)	3000-3115	3055.24
N-Monosubstituted Amine (N-H - in plane bending)	1515-1570	1523.76
Non-conjugated acid (C=O stretching)	1690-1755	1656.85

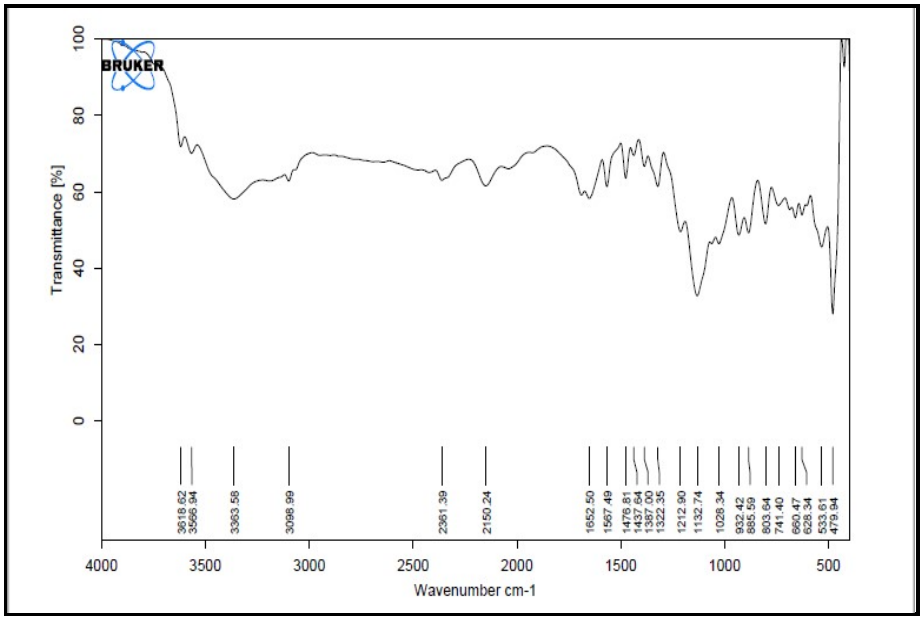


Figure-4.2. FTIR spectrum of RSNa

Table-4.3. Characteristic peaks of RSNa in FTIR

Functional Groups	**Reported Range (cm^{-1})**	**Observed Value (cm^{-1})**
Monosubstituted pyridine (C-H stretching)	3000-3100	3095.75
Phosphorous Acid (OH bending)	1585-1740	1639.49
Phosphorous Acid (OH undefined)	2080-2350	2148.7
Phosphorous Acid (OH stretching)	2525-2780	2611.62
Phosphorous Acid (P=O stretching)	910-1040	931.62
C-P bond (C-P Stretching)	600-800	659.75

4.3.4. DSC analysis:

The thermal behaviour of drugs upon heating was analysed by DSC analysis. The DSC thermogram of ATO and RSNa is shown in figure-4.3 (a) and 4.3 (b) respectively. In case of ATO, a sharp endothermic peak was observed at 166.19 °C

and in case of RSNa, sharp endothermic peak was observed at 253.2 °C. Thus, results confirmed the authenticity of the drug samples.

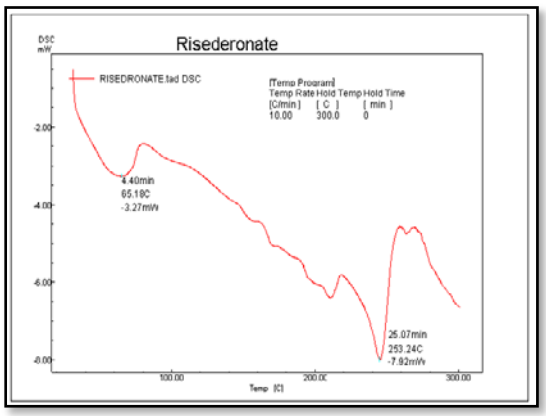


Figure-4.3. (a) DSC of RSNa

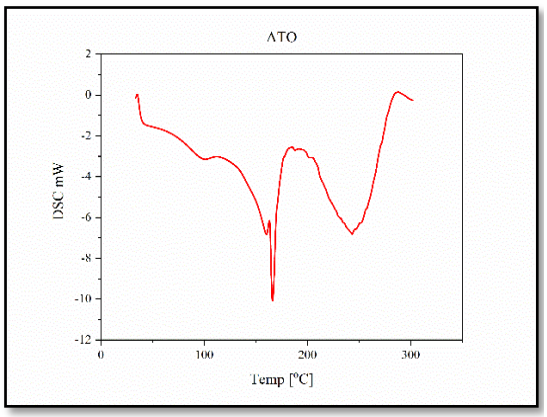


Figure-4.3. (b) DSC of ATO

4.3.5. Determination of λ_{max} by UV-Vis Spectrophotometer:

The λ_{max} for ATO in methanol was found to be 246 nm while in case of RSNa, it was found to be 262 nm in double distilled water which was reported in respective solvents. As a result, the drugs were authenticated.

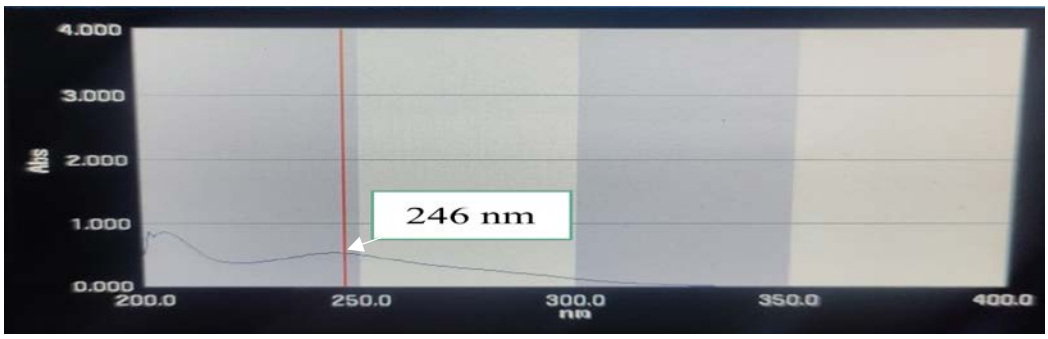


Figure: 4.4 (a) UV spectra of ATO in methanol

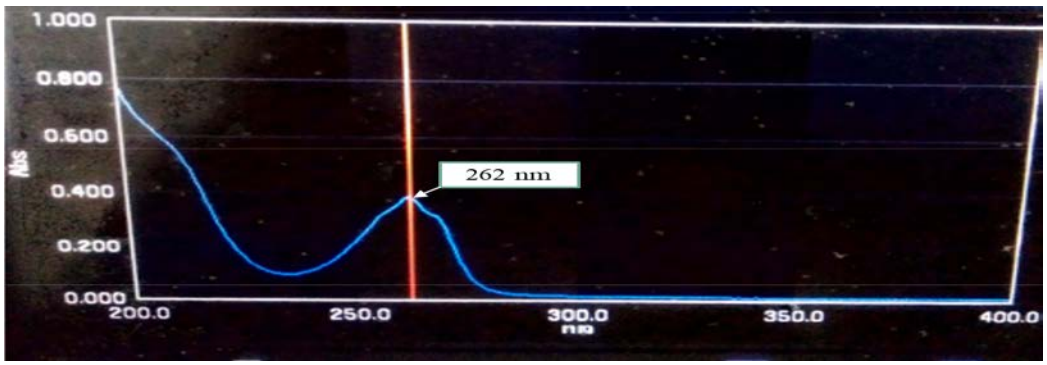
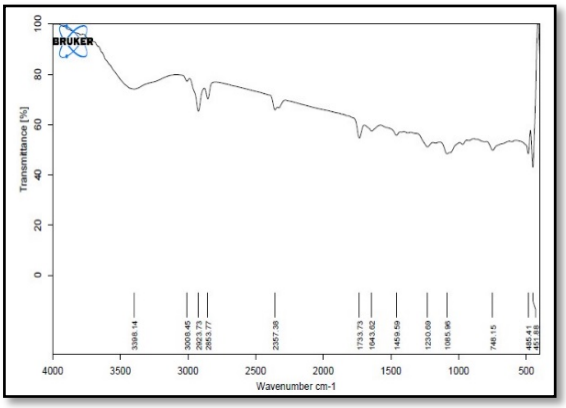


Figure 4.4 (b) UV spectra of RSNa in water

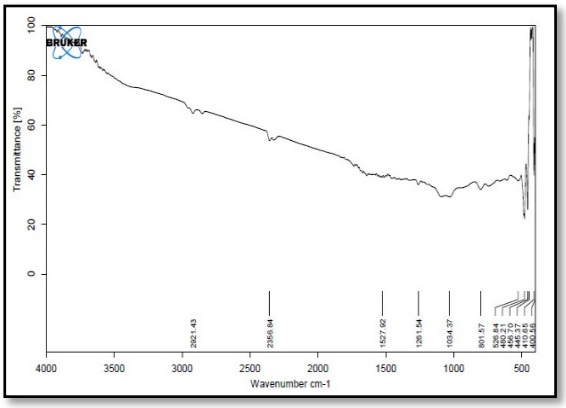
4.4. Drug-excipients compatibility study:

The FTIR spectra of drug-excipients are shown in figure- 4.4. All characteristic peaks pertaining to drugs were prominently observed in IR spectra of physical mixture. The results of compatibility study revealed that no interaction was found between drugs (ATO and RSNa) and excipients used in the formulation.

For glycerosomes

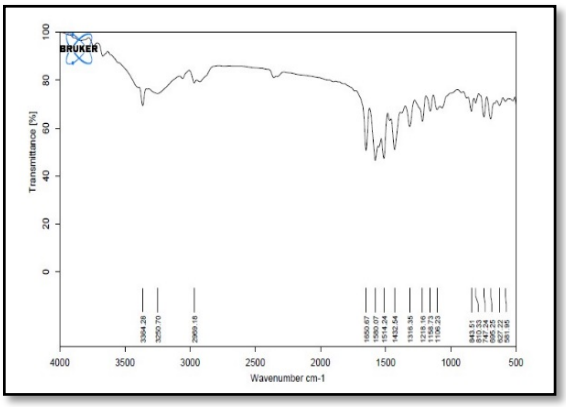


a. Lipoid S-75



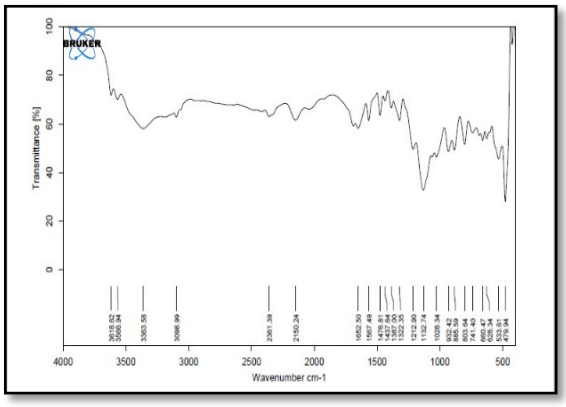
b. Cholesterol

For ATO loaded glycerosomes

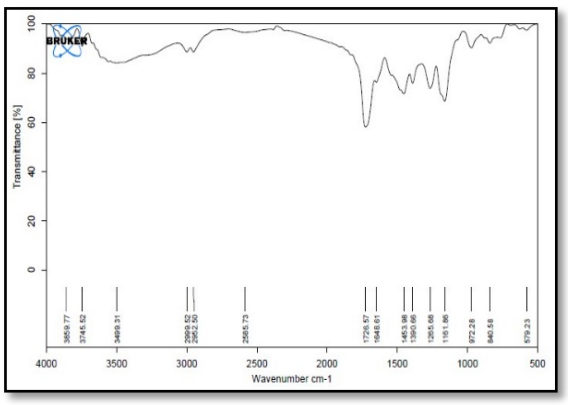


c. ATO

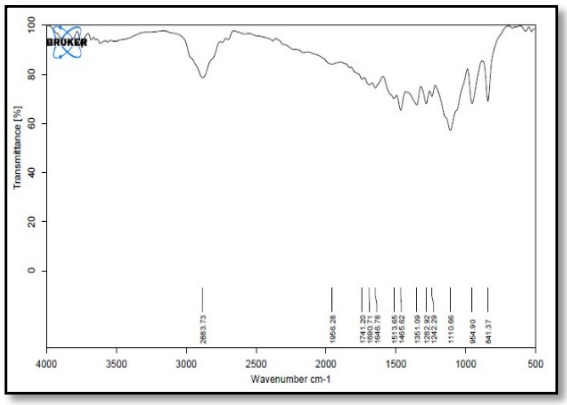
For RSNa loaded glycerosomes



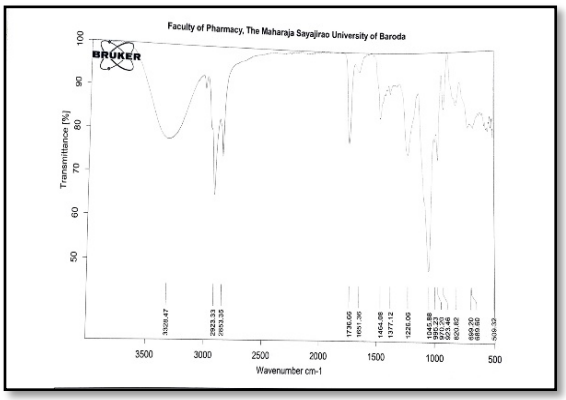
d. RSNa



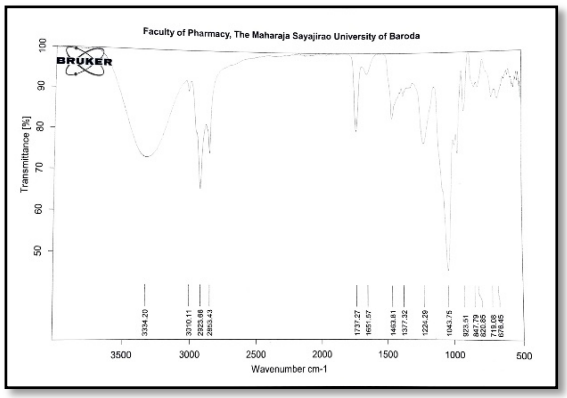
e. ATO + Lipoid S-75



f. RSNa + Lipoid S-75

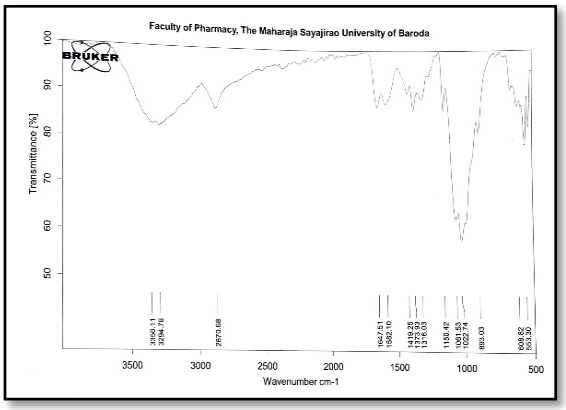


g. ATO + Lipoid S-75 + Chol + Glycerol

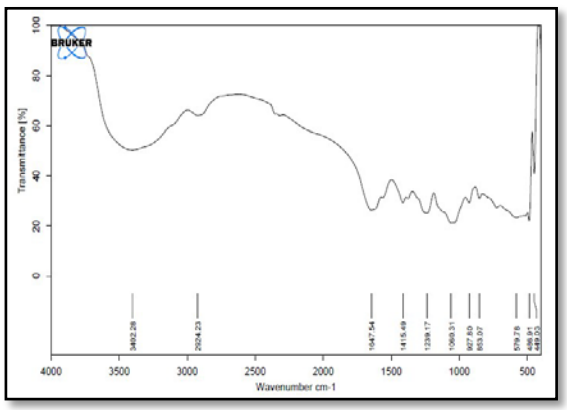


h. RSNa + Lipoid S-75 + Chol + Glycerol

For polyelectrolyte complex nanoparticles (PECN)

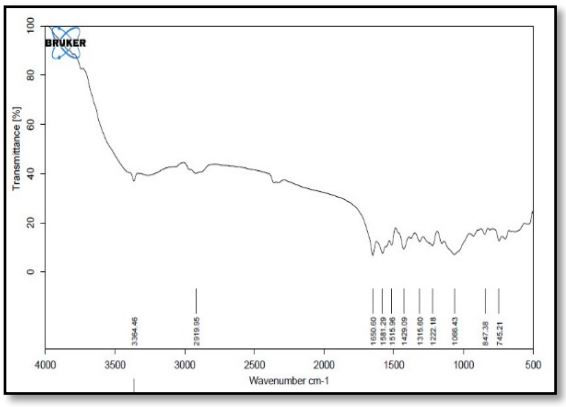


i. Chitosan (CS)

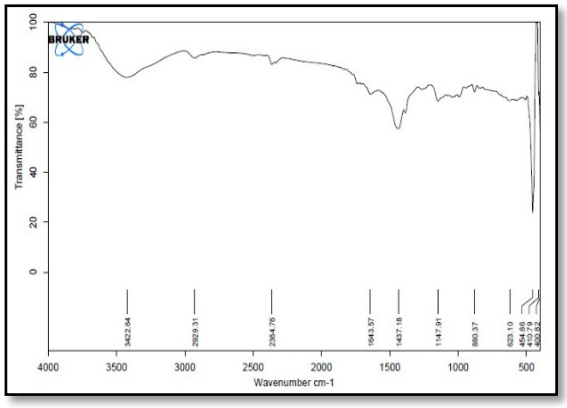


j. Chondroitin sulfate (CHON)

ATO loaded PECN **RSNa loaded PECN**

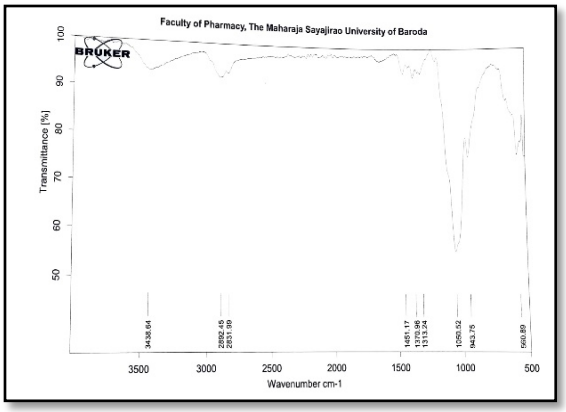


k. ATO + Chitosan + CHON

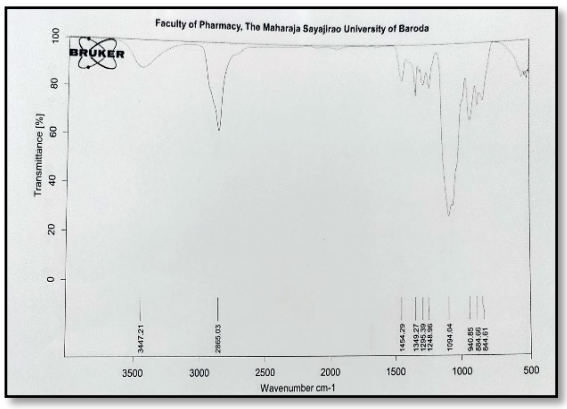


l. RSNa + Chitosan + CHON

Transdermal Patch

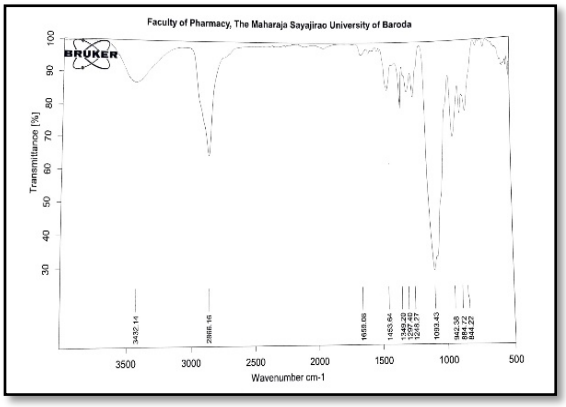


m. HPMC K4M

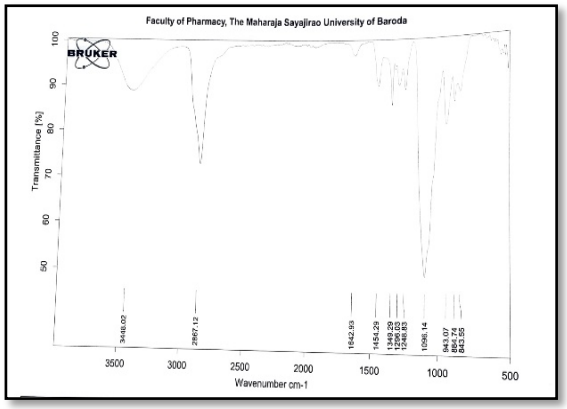


n. PEG 400

ATO TP **RSNa TP**



o. ATO + HPMC + PEG 400



p. RSNa + HPMC + PEG 400

Figure-4.4. Drug-Excipient interaction studies by FTIR

a. Lipoid S-75
b. Cholesterol
c. ATO
d. RSNa
e. ATO + Lipoid S 75
f. RSNa + Lipoid S 75
g. ATO + Lipoid S 75 + Cholesterol + Glycerol
h. RSNa + Lipoid S 75 + Cholesterol + Glycerol
i. Chitosan
j. Chondroitin sulfate
k. ATO + Chitosan + CHON
l. RSNa + Chitosan + CHON
m. HPMC K 4 M
n. PEG 400
o. ATO + HPMC K 4 M + PEG 400
p. RSNa + HPMC K 4 M + PEG 400

Chapter 4 – Preformulation study

4.5. References:

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