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Drug-Excipient Interaction Study of Lornoxicam with Polymers

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Abstract: Interaction study is the most important step in reformulation study for the preparation of all dosage forms. The interaction can affect physical, chemical, therapeutic and biological properties and stability of drug and create a new surprise problem, the successful formulation of stable and effective solid dosage form depends on the careful and suitable choice of excipient. Also the selection of excipient is vital in the design of a quality drug product. The quality of medicine depends not only on the active principals and productions process, but also on the performance of the excipients .The present work shows the interaction study of Lornoxicam and polymers for Nano products. In IR the interaction of infrared radiation with matter. It covers range of techniques, mostly based on absorption spectroscopy. DSC is a thermo-analytical technique in which the difference in the amount of heat required to increase the temperature of sample and reference is measured as a function of temperature.
Keywords: Interaction study, Differential scanning colorimetry (DSC), Infrared spectrophotometric study (IR).

INTRODUCTION

For the development in stage of dosage form, the study of drug-excipient compatibility is an important process. Incompatibility between drugs and excipient, alter the drugs stability and bioavailability and hence it affect their safety and efficacy. Excipient plays important role for preservation of product. The successful formulation of stable and effective solid dosage form depends on the careful and suitable choice of excipient. Also the selection of excipient is vital in the design of a quality drug product.

Also in dosage form, their may be a chances of unintended physicochemical interaction of an excipient with drug substance, thereby it can result in complexation or binding of drug, resulting slow or incomplete drug release in dissolution medium. The excipient and there concentration selected in formulation on the basis of their functionality as well as compatibility between drug and excipient [1].

Effect of drug-Excipient Interaction on Dosage form:

Dosage form is combination of drugs and non-drug components called as excipients. Drug is a chemical substance obtained from natural, synthetic or semi-synthetic source, which is used for the treatment, curing, prevention of disease or disorders in humans as well as animals. Excipients are nondrug components which are serve specific purposes like shape, stability, solubility, elegance, palatability, etc. of dosage form. The quality of medicine depends not only on the active principals and productions process, but also on the performance of the excipients [2].

Techniques to evaluate drugs- excipient compatibilities are-

- Thermal analysis
- Differential scanning colorimetry (DSC)
- Infrared spectrophotometric study (IR)
- Isothermal Stress testing (IST)
- High Performance Liquid Chromatography (HPLC)
- Thin Layer Chromatography (TLC) [3-7]

Thermal Analysis

Branch of materials science where the properties of materials are studied as they change with temperature.

Several methods of Thermal Analysis are

- Dielectric thermal analysis (DEA)
- Differential Thermal Analysis (DTA)
- Dilatometry
- Dynamic mechanical Analysis (DMA)
- Evolved Gas Analysis (EGA)
- Laser Flash Analysis (LFA)
- Thermogravimetric nalysis (TGA)
- Thermomechanical Analysis (TMA)
- Thermo-Optical Analysis (TOA) [7,8,14,15]

Differential scanning colorimetry (DSC)

It is a thermo-analytical technique in which the difference in the amount of heat required to increase the temperature of sample and reference is measured as a function of temperature. Both the samples and reference are maintained at nearly the same temperature through out the experiment. Generally, the temperature program for a DSC analysis is designed such that the sample holder temperature increases linearly as function of time. The reference sample should have a well defined heat capacity over the range of temperature to be scanned.

Types of DSC

- Power compensated DSC, keeps power supply constant.
- Heat flux DSC, keeps heat flux constant [9,10]

Infrared Spectroscopy (IR Spectroscopy or Vibrational Spectroscopy)

It involves the interaction of infrared radiation with matter. It covers range of techniques, mostly based on absorption spectroscopy. For a given sample which may be solid, liquid or gaseous, the method or techniques of infrared spectroscopy uses and instrument called an Infrared Spectrophotometer to produce an infrared spectrum. A basic IR spectrum is essentially a graph of infrared light absorbance (or Transmittance) on the vertical axis vs. Frequency or wavelength on the horizontal axis.

Isothermal Stress Testing

In Isothermal stress testing, drug and different excipients were weighed directly in 4mL-glass vials (n=2) and mixed on a vortex mixer for 2 min. In each of the vials, 10 % (w/w) water was added and drug excipients blend was further mixed using a glass capillary (both the ends of which were heat sealed). To prevent any loss of materials, the capillary was broken and left inside the vial. Each vial was sealed using a Teflon-lined screw cap and stored at 50 ^{o} C in a hot air oven. These samples were periodically examined for any unusual color change. After 3 weeks storage under the above conditions, samples were quantitatively analyzed using UV-visible Spectrophotometer [11, 12].

Drug -Excipients Interaction Study

The drug-excipients interaction study was carried out using FT-IR and DSC

Fourier Transform-Infrared spectroscopy (FTIR)

FTIR spectra of Lornoxicam, precirol ATO5 (PRE) and physical mixture of lipids with Lornoxicam were studied. Above samples were mixed with KBr of IR grade in the ratio of 1:100 and compressed using motorized pellet press (Kimaya Engineers, India) at 10-12 tones pressure. The pellets were then scanned using FTIR spectrophotometer (Shimadzu 8400S, Japan). The FTIR spectra of mixtures were compared with that of the FTIR Spectra of pure drug and lipid, to confirm any change occurs or not in the principle peaks of spectra of plain drug and lipid [13].

Differential Scanning Calorimetry Study

Thermal analysis was carried out for Lornoxicam, PRE and physical mixture of them were conducted using DSC (Mettler DSC 1 star system, Mettler-Toledo, Switzerland) at a heating rate of 10°C /min. The measurements were performed at a heating range of 40 to 300°C under nitrogen atmospheres.

Differential Scanning Calorimetry (DSC)

Lornoxicam was confirmed by differential scanning calorimetry at scanning rate of 10^{o}C/min, it exhibits a sharp melting exothermic peak at temperature of 220.66^{0}C as shown in Figure 10. The sharp intense exothermic peak indicates the crystalline nature of drug.

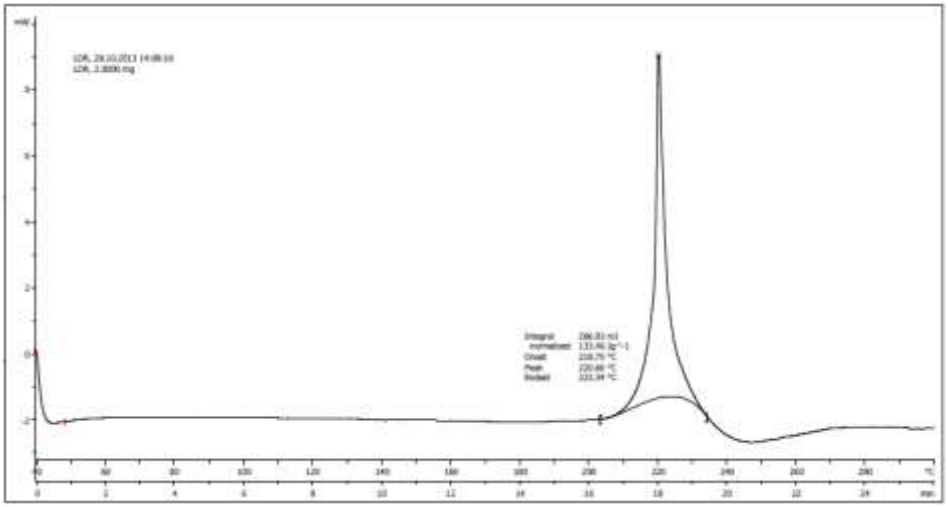


Fig-1: DSC Thermogram of pure Lornoxicam

Infrared Spectrum (FTIR)

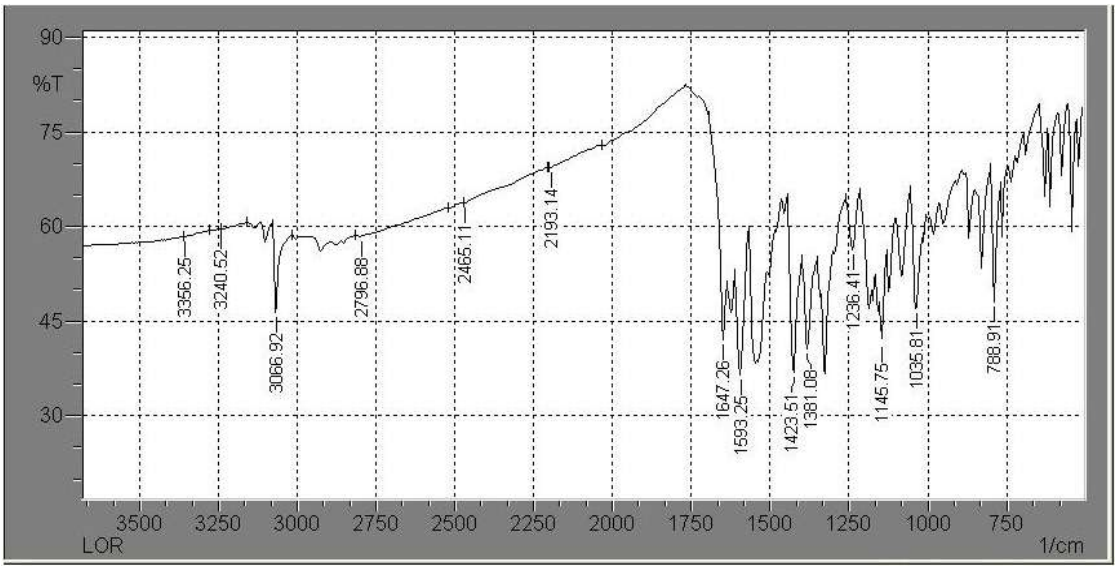


Fig-2: Infrared spectrum of Lornoxicam

The IR spectrum was measured in the solid state as potassium bromide mixture. The IR spectrum of Lornoxicam is shown in Figure 2. Principal peaks and chemical group present in IR spectra of Lornoxicam is shown in Table 1.

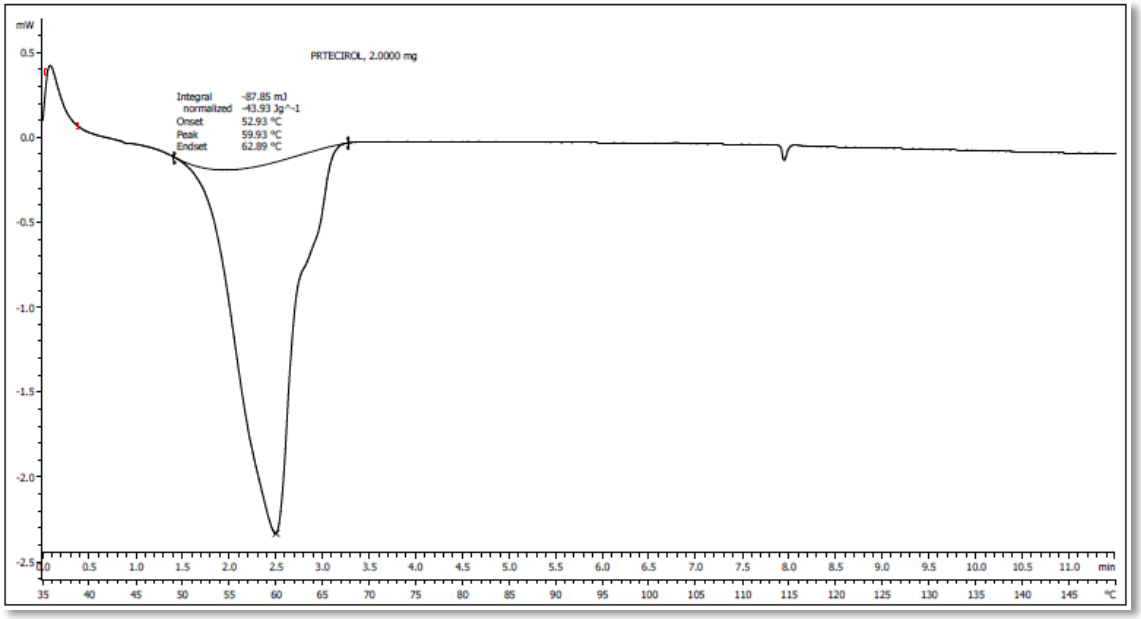
Table-1: Principal peak and chemical group present in IR spectra of Lornoxicam.

Sr.no.	Reported peaks (cm^{-1})	Observed peaks (cm^{-1})	Interpretation of the peaks (Functional Group)
1	3500-3180	3240.52	N-H stretch amide
2	3100–3000	3066.92	C–H stretch aromatics
3	1680–1640	1647.26	–C=0 Stretching Carbonyl
4	1600–1585	1593.25	C–C stretch aromatics
5	1200-1025	1145.75	C-N Stretch amine

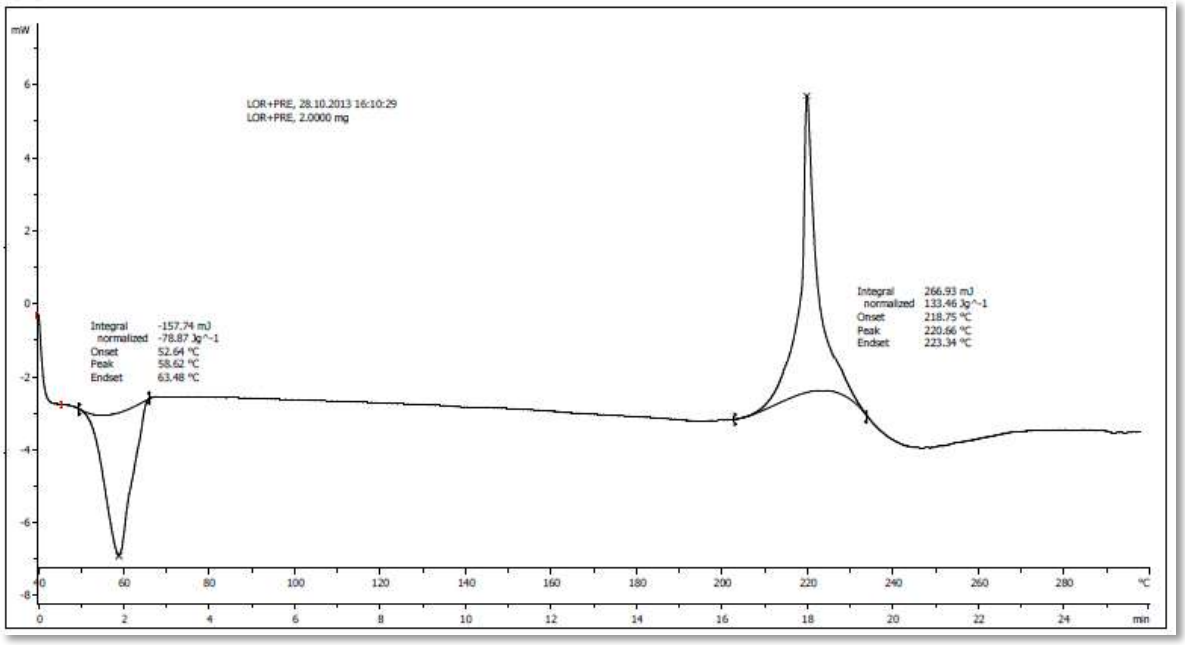
Drug Excipients Interaction Study

Differential Scanning Calorimetry (DSC) study

The DSC thermograms were recorded for Lornoxicam, bulk Precirol and mixtures of Lornoxicam with precirol. The DSC heating and cooling curves were recorded as a plot of enthalpy (in mW) vs. the temperature in (°C). For the Lornoxicam, the melting process took place at 218.75°C with maximum peak at 220.66°C and for bulk material of precirol melting process took place at 52.93°C with maximum peak at 59.93°C**.** No significant change in the position of peaks was observed after running the physical mixture (1:1) of drug and solid lipid (figure 3). Thus, physical incompatibility between the components was discarded.



Fig–3: DSC Thermogram of Precirol



Fig–4: DSC thermogram of physical mixture containing Lornoxicam and Precirol in 1:1 ratio

Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectra of Lornoxicam, Precirol, and physical mixture are shown in fig.5, 6, 7, respectively and their interpretation is in Table 10. From interpretation it can be concluded that there is no drug polymer interaction.

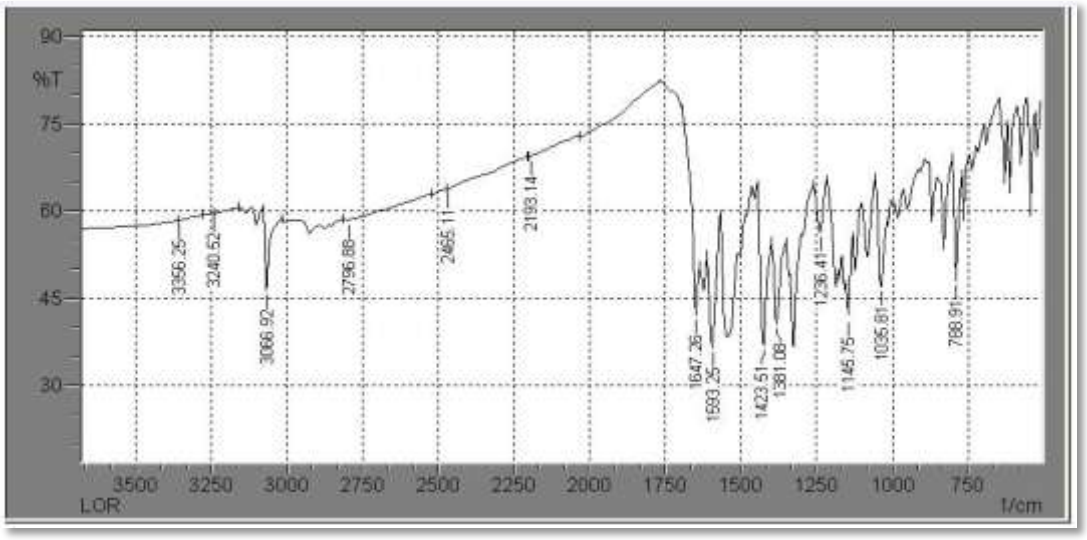


Fig-5: Infrared spectrum of Lornoxicam

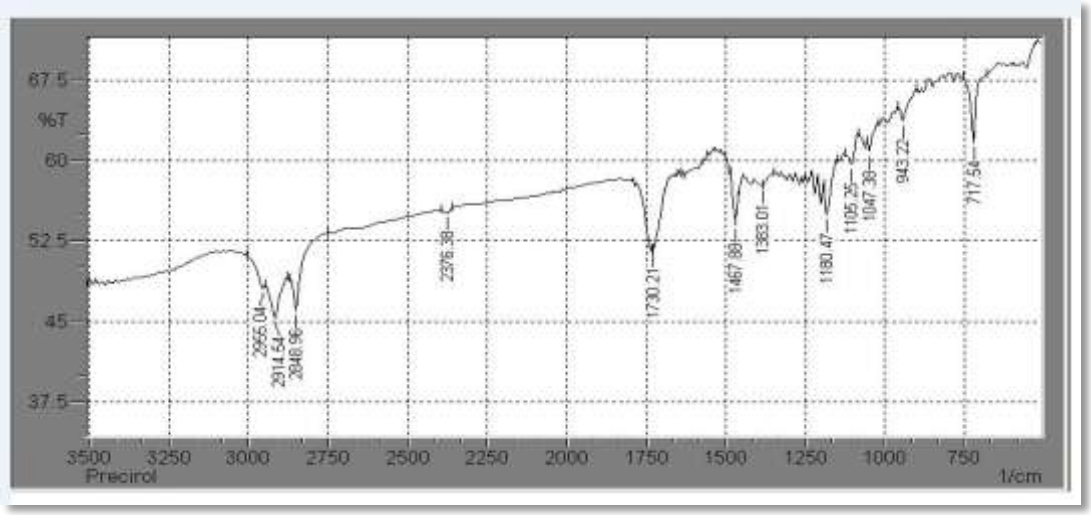


Fig-6: Infrared spectrum of Precirol

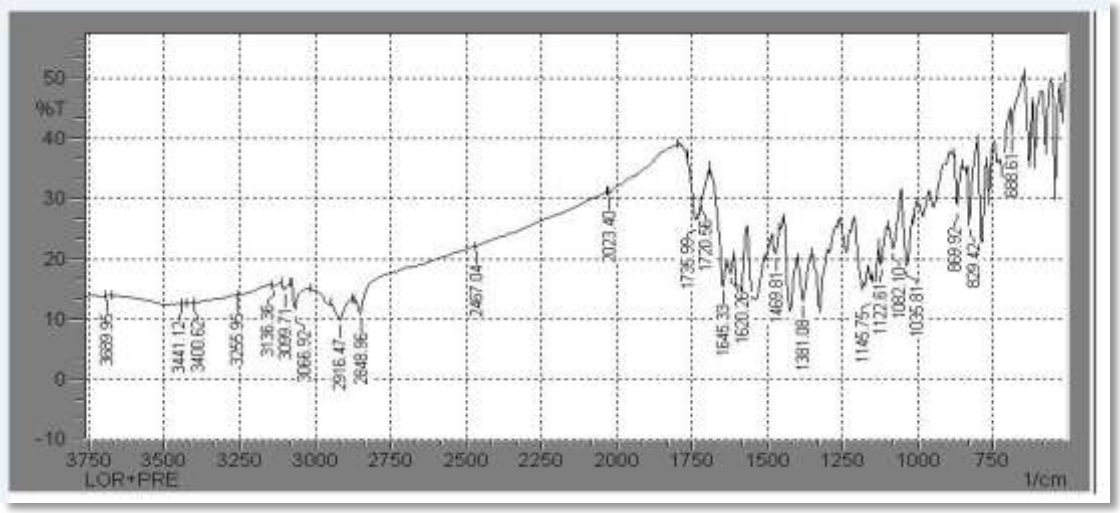


Fig-7: Infrared spectrum of physical mixture

Table-2: Drug Polymer Interaction Studies by IR Spectroscopy

	Wavenumbers of observed peaks (cm^{-1})			
1	Lornoxicam	Precirol ATO5	Physical Mixture	Interpretation of the peaks
2	3066.92	2914.54	3066.92	No Interaction
3	1647.26	2848.96	2848.96	No Interaction
4	1593.25	1730.21	1735.99	No Interaction
5	1423.51	1467.88	1645.33	No Interaction
6	1381.08	1383.01	1469.81	No Interaction
7	1236.41	1180.47	1381.08	No Interaction
8	1145.75	1105.25	1145.75	No Interaction
9	1035.81	1047.38	1035.81	No Interaction

FTIR spectra were recorded for Lornoxicam, Precirol, and physical mixture. Pure Lornoxicam spectra showed sharp characteristic peaks at 3066.92, 1647.26, 1381.08, 1145.75, 1035.81cm-1. All the above characteristic peaks of drug appeared in the spectra of the physical mixture at the same wave number indicating no modification or interaction between the drug and the polymer.

CONCLUSION

Drug-excipient interaction study plays important role for the stability, safety and efficacy of dosage form, with the help of FTIR and DSC, it was concluded the drug and excipient are compatible with each other hence does not show any interaction in the preparation of dosage form.

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