Research Article

Study of Physicochemical Compatibility of Inhalation Grade Active Ingredients with Propellant HFA 134a by FTIR

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ABSTRACT

The studies of drug-excipient compatibility represent an important phase in the preformulation stage of the development of all dosage forms. The purpose of present study to identify the physicochemical compatibility of hydrofluoroalkane (HFA) propellant 134a with inhalation active ingredients viz; Salmeterol Xinafoate, Fluticasone Propionate, Anhydrous Beclometasone Dipropionate and Salbutamol Sulfate by Fourier Transform Infrared Spectrophotometer (FTIR) method of analysis. The potential physical and chemical interactions between inhalation drugs and suspending agents like Propellant 134a can affect the chemical, physical properties and stability of the Pressurized Metered Dose Inhalers. The present work contains a basic mode of drug degradation, mechanism of drug-propellant interaction like physical, chemical and biopharmaceutical. Once the type of interaction is determined we can take further steps to improve the stability of pressurized metered dose inhalers suspension formulations. In this study report FTIR studies were performed and major peaks were determined by the (FTIR Bruker) will show band shift and broadening compared to the spectra of pure drug. IR spectra's of Salmeterol Xinafoate, Fluticasone Propionate, and Anhydrous Beclometasone Dipropionate and Salbutamol Sulfate bands were found appropriate wavelength and this confirms the identity of individual API.

Keywords: Drug-Excipient Compatibility, Incompatibility, FTIR, Propellant HFA 134a.

INTRODUCTION

A Complete characterization and understanding of physicochemical interactions of an active pharmaceutical ingredient (API) in the dosage forms is an integral part of preformulation stage of new dosage form development as it is most desirable for consistent efficacy, safety and stability of a drug product. In pressurized metered dose inhalers, an API comes in direct contact with other components (propellants) of the formulation that facilitate the administration and release of an active component from the canister. Although propellants are chemically and pharmacologically inert, they can interact with drugs in the formulation to affect drug product stability in physical aspects such as organoleptic properties, deposition at site of action reduces or chemically by causing drug degradation.[1, 2.]

Mechanism of Drug Excipient Interaction

Exact mechanism of drug excipients interaction is not clear. However, there are several well documented mechanisms in the literatures. Drug excipients interaction occurs more frequently than excipient-excipient interaction. Drug excipients interaction can either be beneficial or detrimental, which can be simply classified as - 1. Physical Interactions and, 2. Chemical Interactions.

Careful selection of the propellants are required for a robust and effective formulation of metered dose inhaler forms that make administration easier, improve patient compliance, promote release and bioavailability of the drug and increase its shelf life. Thus, compatibility screening of an API with excipients or other active ingredients is recognized as one of the mandatory factors and is at the fore front of drug product science and technology research.

A complete understanding of the physicochemical interactions in dosage forms is expected under quality by design prototype of drug development. The analytical methods into the initial steps of preformulation studies have contributed significantly to early prediction, monitoring and characterization of the API incompatibility to avoid costly material wastage and considerably reduce the time required to arrive at an appropriate product formulation. The purpose of the current investigation was to evaluate and identify the physicochemical compatibility of hydrofluoroalkane (HFA) propellants 134a & 227ea with various inhalation active ingredients viz; salmeterol xinafoate, fluticasone propionate, anhydrous beclometasone dipropionate and salbutamol sulfate to be used in the metered dose inhaler formulations utilizing the by Fourier Transform Infrared Spectroscopy.[4]

MATERIALS AND METHODS

The various inhalation active ingredients were procured from the Vamsi Labs Ltd. Solapur, India. The HFA Propellants 134a was obtained from E I DuPont, USA. 50µl Metered Valve was obtained from Aptar, China and 19ml aluminium canisters was obtained from Presspart, UK.

To confirm the physicochemical interactions between inhalation APIs (Salmeterol Xinafoate, Fluticasone

Propionate, Anhydrous Beclometasone Dipropionate and Salbutamol Sulfate) with Propellant HFA 134a. IR spectra's were recorded on a FTIR spectroscopy using the instrument FT-IR Bruker in the frequency range of 400-4000 cm^{-1} with the resolution of 4 cm^{-1}. The individual samples of drugs as well as the mixture of various drug and propellant HFA134a were filled in aluminium canister, mixed content of filled canister by sonicate for 3-5 mins in a sonicator. FTIR studies were performed by FTIR-(Bruker) of individual drug samples and the mixture of drug with propellant HFA 134a; the results were compared to know the possible interaction.[3-5]

RESULTS AND DISCUSION [4-6]

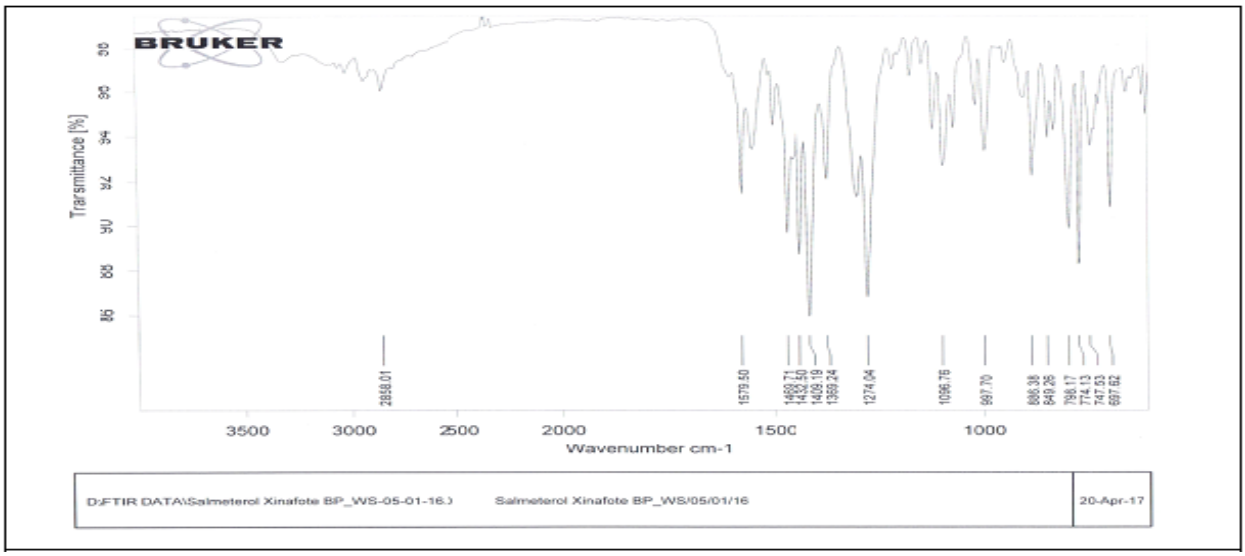

Figure 1: Standard FTIR Spectrum of Salmeterol Xinafoate BPCRS

FT-IR Spectrums of Salmeterol Xinafoate, the principle peaks are obtained at various wavelengths 1409cm^{-1} - (OH) Alcoholic Bend for Hydroxyl group, 1580 cm^{-1}- (>N-H) Bend for Secondary Amine, 1650cm^{-1}- (C=C) for Alkene Stretch and Alkenes, 883 cm^{-1} - (C-O) Stretch for Ether Group, 1080cm^{-1} - (C-O-C) Stretch for Polysaccharides, 3400 cm^{-1} - (C-OH) Stretch for Alcoholic group, 884cm^{-1} - (C-H) Bend for Aromatic Benzene Ring, 1320 cm^{-1} - (C-N) Stretch for Aromatic Prim, 3000cm^{-1} - (C-H) Stretch for Methylene group **(Ref. Fig.01)**.

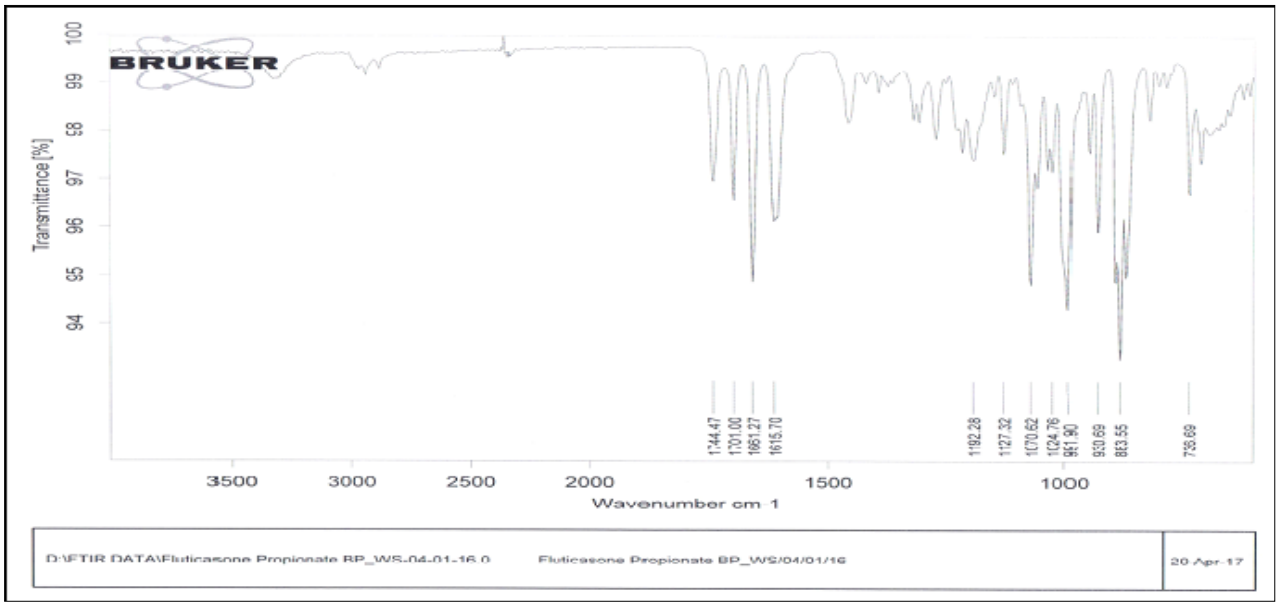

Figure 2: Standard FTIR Spectrum of Fluticasone Propionate BPCRS

FT-IR Spectrums of Fluticasone Propionate, the principle peaks are obtained at wavelengths; 1409 cm^{-1} - (OH) Stretch for Hydroxyl group, 1661 cm^{-1} (C=C) Stretch, Aromatic ring, 991cm^{-1} (S-H) Thiol Stretch for Thiol Group, 1024 cm^{-1} (C-F) for Fluorine, 883 cm^{-1} - (C-O) Stretch for Ether Group, 930 cm^{-1} - (C-H) Bend for 5 Items ring, 736 cm^{-1} - (C-H) Bend for Aromatic Benzene Ring, 1715 cm^{-1} - (C=O) for Ketones, 3000 cm^{-1} - (C-H) Stretch for Aldehyde **(Ref. Fig.02)**.

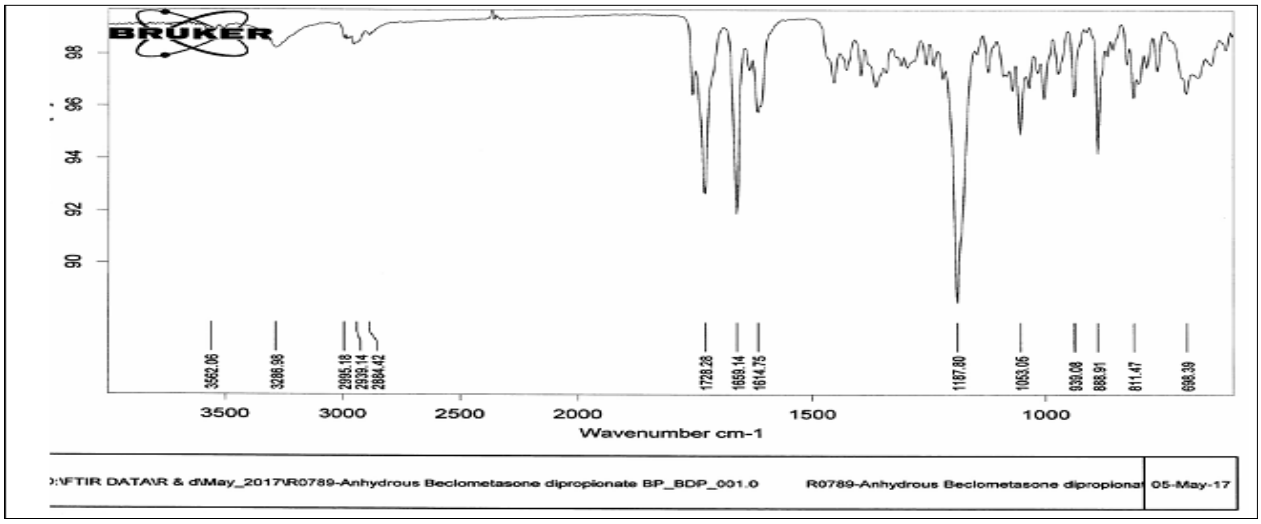

Figure 3: Standard FTIR Spectrum of Anhydrous Beclometasone Dipropionate BPCRS

FT-IR Spectrums of Anhydrous beclometasone Dipropionate, the principle peaks are obtained at wavelengths; 1409 cm^{-1} -(OH) Alcoholic Bend for Hydroxyl group, 1715 cm^{-1} (>C=O) for Very Strong Stretching & Vibrations, Ketones, 1650 cm^{-1} - (C=C) Alkene Stretch for Alkenes, 1659 cm^{-1} (C=C) for Stretching & Vibration, 1080 cm^{-1} - (C-O-C) for Stretch & Polysaccharides, 3400 cm^{-1} (C-OH) for Stretch, Alcoholic group, 1053 cm^{-1} - (Ar-C-Cl) for Stretching and Vibration, Aromatic Benzene Ring, 3000 cm^{-1} - (C-H) for Stretch, Methylene, 930 cm^{-1} - (C-H) for Bend, 5 Items ring **(Ref. Fig.03)**.

FT-IR Spectrums of Salbutamol Sulphate, the principle peaks are obtained at wavelengths; 1409 cm^{-1}, - (OH) for Bending & Hydroxyl group, 1661 cm^{-1} - (C=C) for Stretch & Aromatic ring, 1100 cm^{-1}, (C-O) for stretch & Ether Group, 1028 cm^{-1} - (C-H) for Bend, Aromatic Benzene Ring, 3000 cm^{-1}, (C-H) for Stretch & Aldehyde, 1650 cm^{-1} - (C=C) for Stretch and Alkenes **(Ref. Fig.04)**.

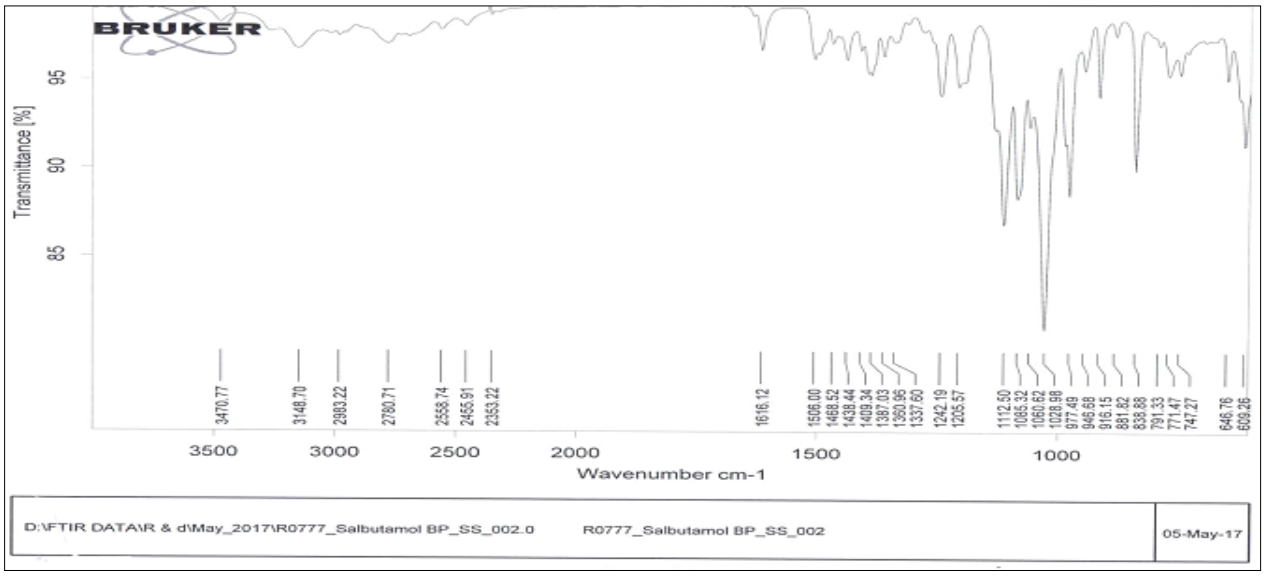

Figure 4: Standard FTIR Spectrum of Salbutamol Sulphate BPCRS

Salmeterol Xinafoate, Fluticasone Propionate and Propellant Compatibility

This study clearly indicates absence of any chemical interaction between the Drug: excipient (Salmeterol Xinafoate and Fluticasone Propionate) Excipient (Propellant HFA 134a) and thus confirming that the drug (Salmeterol Xinafoate and Fluticasone Propionate) are compatible with the excipient used in the present formulation. However, the intensity of the some peaks were slightly decreased in the FTIR spectrum of the physical mixture due to the intermolecular hydrogen bonding between drug and excipient, indicating the chemical stability of the drug with each other and excipient **(Ref. Fig.05)**.

This confirms the identity of Salmeterol and Fluticasone by indicated characteristic peaks belonging to major functional groups which are similar to standard peaks.

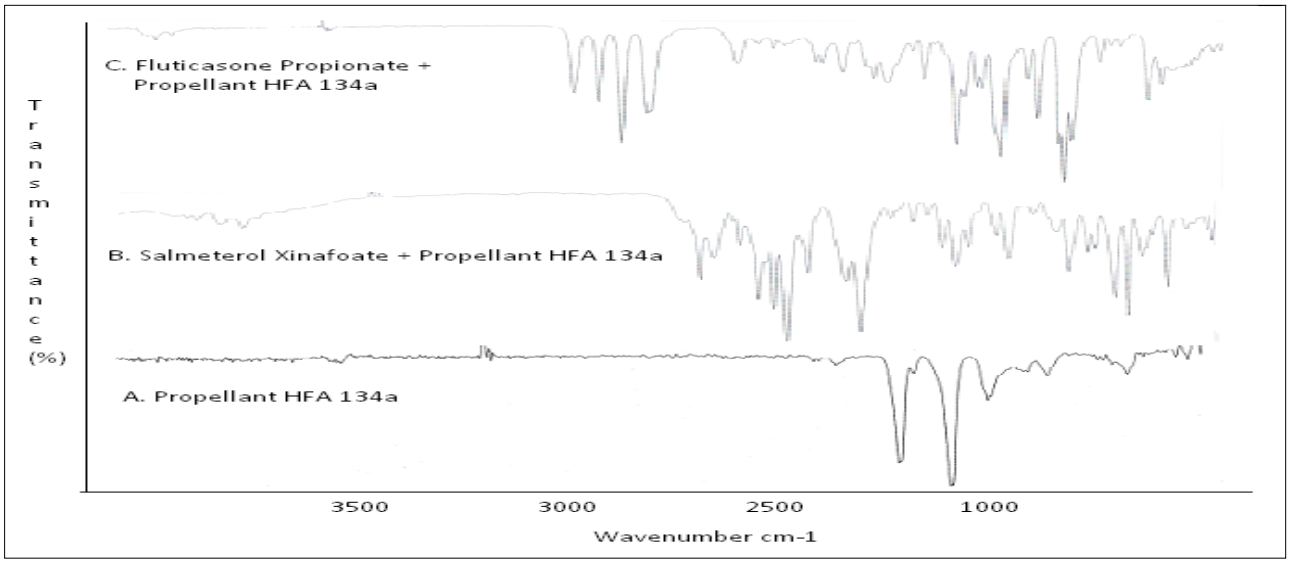

Figure 5: FTIR Spectrum, Mixture of Fluticasone, Salmeterol and Propellant HFA 134a

Anhydrous Beclometasone Dipropionate and Propellant Compatibility

The results reveal that, Beclometasone Dipropionate has no interaction with propellant 134a and clearly indicates absence of any chemical interaction between the Drugs: Excipient (Propellant HFA 134a) and thus confirming that the drug (Anhydrous Beclometasone Dipropionate) is compatible with the propellant used in the present formulation **(Ref. Fig.06)**.

However, the intensity of the some peaks were slightly decreased in the FTIR spectrum of the physical mixture due to the intermolecular hydrogen bonding between drug and excipient, indicating the chemical stability of the drug with excipient.

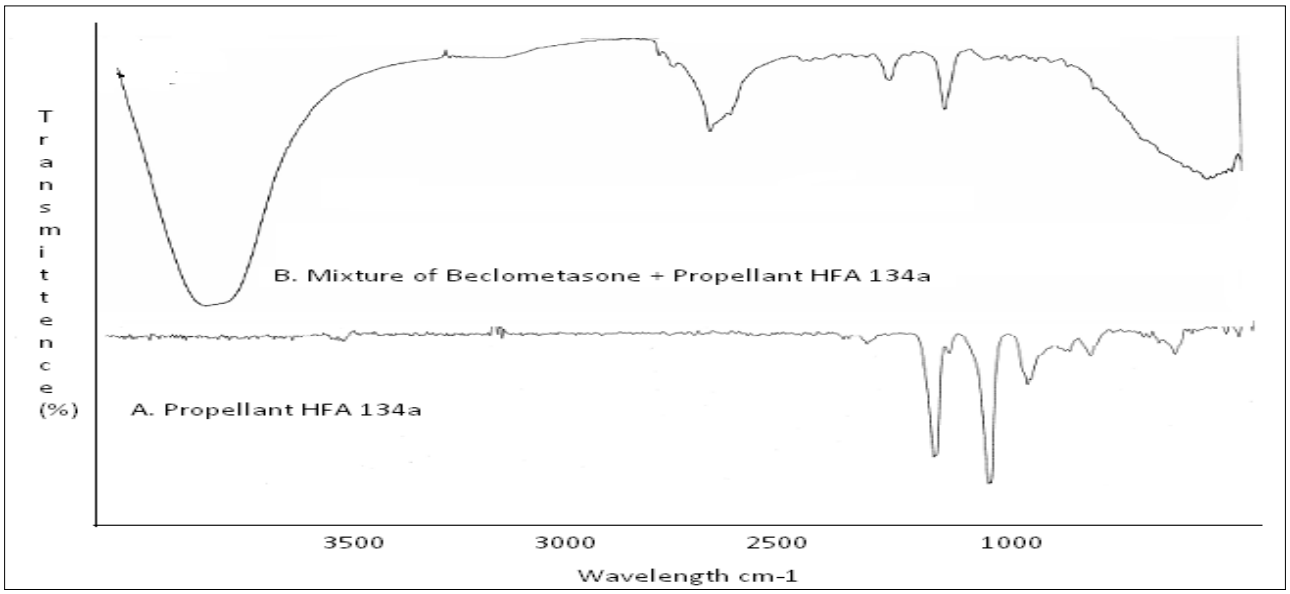

Figure 6: FTIR Spectrum, Mixture of Beclometasone Dipropionate and Propellant HFA 134a

Salbutamol Sulphate and Propellant Compatibility

The result indicates that, Salbutamol Sulphate has no interaction with propellant 134a there is an absence of any chemical interaction between the Salbutamol and the Propellant HFA 134a. Thus, confirming that the Salbutamol Sulphate is compatible with propellant 134a used in the present formulation **(Ref. Fig.07)**.

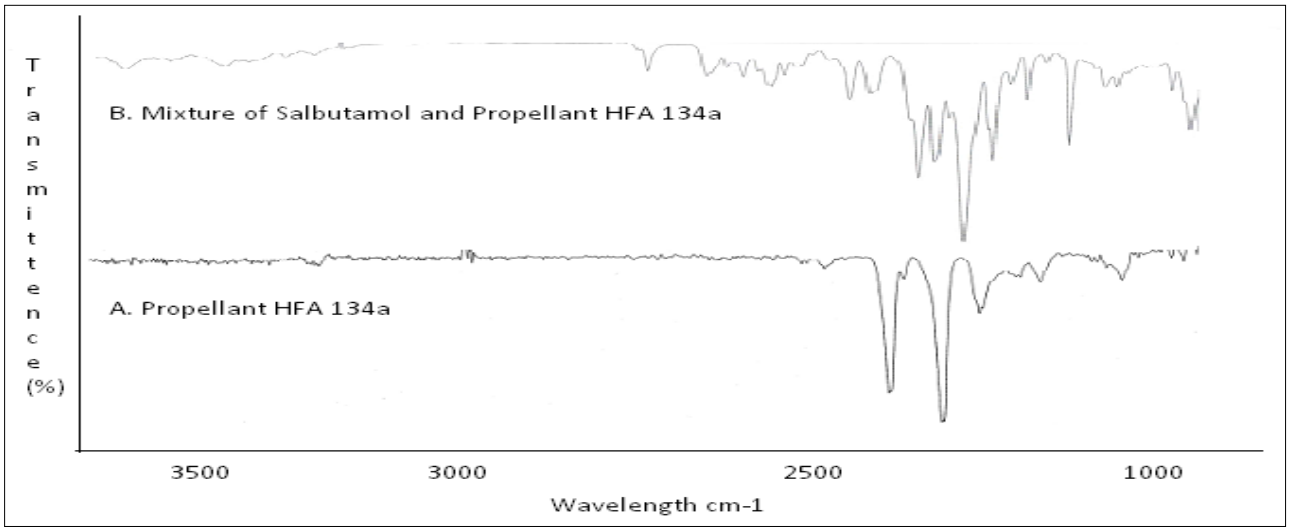

Figure 7: FTIR Spectrum, Mixture of Salbutamol and Propellant HFA 134a

CONCLUSION

The compatibility of propellant HFA 134a with various inhalation active pharmaceutical ingredients (API) was studied by Fourier Transform Infrared Spectroscopy Testing. In the present study, results of FTIR were successfully employed to assess the compatibility of Propellant HFA 134a with the inhalation APIs. The study clearly indicates absence of any chemical interaction between the Drugs (salmeterol xinafoate, salbutamol sulfate, anhydrous beclometasone dipropionate, and fluticasone propionate) and Excipient (Propellant HFA 134a) and thus confirming that they are compatible with each other. However, the intensity of the some peaks were slightly decreased in the FTIR spectrums of the physical mixtures due to the intermolecular hydrogen bonding between drug and excipient, indicating the chemical stability of the drugs with excipient (Propellant HFA 134a).

Hence, this data's attests the potentiality of the excipients for the successful development of a pressurised metered dose inhaler formulation containing salmeterol xinafoate, salbutamol sulfate, anhydrous beclometasone dipropionate, and fluticasone propionate with the suspending agent Propellant HFA 134a.

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