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CO–CRYSTAL SYNTHESIS AND STRUCTURAL ANALYSIS OF PARACETAMOL AND 3–NITROBENZOIC ACID

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ABSTRACT:

Co-crystal are being studied largely in the modern day because they have the ability to modify the physical properties of solid state materials particularly pharmaceuticals. cocrystals has in necessitated additional research on methods to make co-crystals that can offer environmentally attractive and effective options. Co-crystallization alters the molecular interaction. They also alter the composition of pharmaceuticals materials. Co-crystals consist of API and stoichiometric amount of acceptable co-crystal forms, Pharmaceutical co-crystals is an approach to find out solubility and dissolution of drugs. Paracetamol is non-steroidal anti-inflammatory drug. The present study aim to increase the solubility of drug and dissolution. Co-crystals can be constructed through several types of interaction, including hydrogen bonding, pi-stacking and wander walls forces.

Keywords : *Co-crystallization, Hydrogen bonding, Co-crystal.*

INTRODUCTION :

In the last few decades, pharmaceutical industry has achieved a great progress in its reach for new drug compounds by applying combinatorial approaches and high throughout in vivo screening. However compounds obtained by such methods typically have a number of defects, the main one being their low solubility in aqueous media and consequently their low bioavailability.[1-5] 40% of drug in the market have low solubility. Therefore it is an have of the need to soluble drug compounds by using innovative techniques. Co-crystals are also proven for as potential intellectual property items which can buying back into the market generic drugs with improved characteristics as unique brand. Physicochemical properties of pharmaceutical can be improved by obtaining cocrystals using co-crystallization.[6-8]

Co-crystallization with pharmaceutical acceptable (GRAS) compounds not affect pharmacological activity of API but can improve physical properties, such as solubility, hygroscopicity, compaction behaviour.[9-11]

The components in a cocrystals exist in a definate stoichiometric ratio, and assemble via non-covalent interaction such as hydrogen bonds, ionic bonds, π-π or vander Waals interaction other than by ion polarity. Co-crystals are an alternative to salts when these do not have appropriate solid state properties or cannot be formed due to the absence of ionization sites in the API.

MATERIALS:

We purchased Paracetamol from the Cipla product and the 3-Nitrobenzoic acid was purchased from loba chemicals pvt. Ltd. and physical examination are given below.

PARACETAMOL

Paracetamol also known as Acetaminophen is a medication used to treat fever and mild to moderate pain. Paracetamol may relieve pain in acute mild migraine but only slightly in episodic tension headache. However, the paracetamol combination helps with both condition where the pain is mild and is recommended as a first-line treatment. Cahn and Hepp or a French

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chemist called Charles Gerhardt first synthesized paracetamol in 1852. Common side effects of paracetamol are nausea and abdominal pain, and it seems to have tolerability similar to ibuprofen.

Paracetamol, an analgesic and antipyretic substances, has slow onset but has a longer duration of action and is lacking anti-inflammatory properties.

During the COVID-19 pandemic it was considered by some in the scientific community that it was an effective analgesic medication to treat symptoms of COVID-19, but this was found to be unsubstantiated.

Formula :- C8H9NO2

Molar mass :- 151.163 g/mol

Melting point :- 169 °C

IUPAC Name :- N-(4-hydroxyphenyl)acetamide, N-(4-hydroxyphenyl)ethanamide.

3-NITROBENZOIC ACID

3-Nitrobenzoic acid is an organic compound with the formula C6H4(NO2)CO2H. It is an aromatic compound and under the standard condition, it is an off- white solid. Two substituents are in a meta position with respect to each other, giving the alternative name of m-nitrobenzoic acid. This compound can be useful as it is a precursor to 3-aminobenzoic acid, which is used to prepare some dyes.

Formula :- C7H5NO4

Molar mass :- 167.12 g/mol

Melting point :- 139 - 141°C

PREPARATION OF CO-CRYSTALS:

Liquid assisted grinding (LAG) as an extension of traditional solvent free mechanochemical techniques by which a small amount is used as an additive to enhance or control reactivity, has been fruitfully applied in the screening of inclusion compound, cocrystals salts, solvates, and polymorphs.

Liquid assisted grinding method was employed to prepare Paracetamol – 3-nitrobenzoic acid co-crystal. A paracetamol is used as a Drug and 3-NBA is used as a coformer were mixed in distinct molar ratio (1:1) in mortar and pestle for 45 min. to develop cocrystals. Ethanol was added dropwise in very small quantity to moisten the mixture of drug and coformer during grinding.[16]

RESULT AND DISCUSSION:

FTIR ANALYSIS:

The IR spectra of Paracetamol Shows the presence of the characteristics peaks which were recorded at 3230 cm^{-1} for stretching of -NH group in primary amide, O-H stretching recorded at 3122 cm^{-1}, C-H stretching at 2972 cm^{-1}, C=O stretching in amide group at 1725 cm^{-1}, aromatic C=C peaks observed at 1645 cm^{-1}, Benzene peak observed at 1350 cm^{-1} and 782 cm^{-1} peaks observed for -C-H of substituted benzene. The IR spectrum of 3- Nitrobenzoic acid revealed an absorption band at 3099 cm^{-1} for =C-H stretching , C=O (acid) stretching shows strong intense peaks at 1685 cm^{-1}, N-O stretching observed at 1533 cm^{-1} and 740 cm^{-1} peak observed for =C-H (bending) of substituted benzene. The IR bands were significantly shifted in the co-crystals in comparison to pure drug and coformer indicating interaction between drug and coformer. In the co-crystals, the new peak recorded at 1725 cm^{-1} and 1689 cm^{-1} for stretching of C=O group and peak for NO_2 group observed at 1345 cm^{-1} supporting the formation of cocrystals.

POWDER X-RAY ANALYSIS:

The fingerprint method to evaluate solid forms is PXRD. The diffractogram of Paracetamol and 3-NBA exhibited characteristic intense diffraction peaks at various 2θ values showing the crystalline nature. The co-crystal showed different extent of crystallinity. The PXRD pattern of the cocrystals was different from Paracetamol or 3-NBA and some additional diffraction peaks were appeared which were not present in the drug or conformer. Hence,

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appearance of new diffraction peaks signals the formation of new crystal-line phase. Cocrystal formation based on the PXRD pattern is well established. The PXRD pattern of cocrystals was different from the pure drug and used to validate formation of new cocrystals.

CONCLUSION:

The supramolecular study of surface analysis of pharmacologically active Paracetamol compound were analyzed using mercury software. It is observed that the title compound crystallizes in monoclinic system in the crystal packing. Paracetamol- 3-Nitrobenzoic acid cocrystal were prepared with paracetamol and 3-Nitrobenzoic acid by liquid assisted grinding method. Cocrystals formation was validated by FTIR and PXRD which jointly supported each other.

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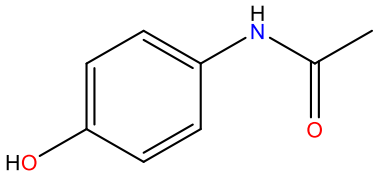

Fig. Structure of Paracetamol

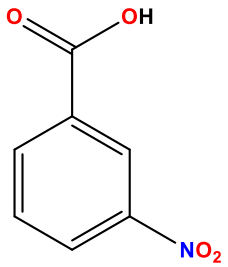

Fig. Structure of 3-Nitrobenzoic acid

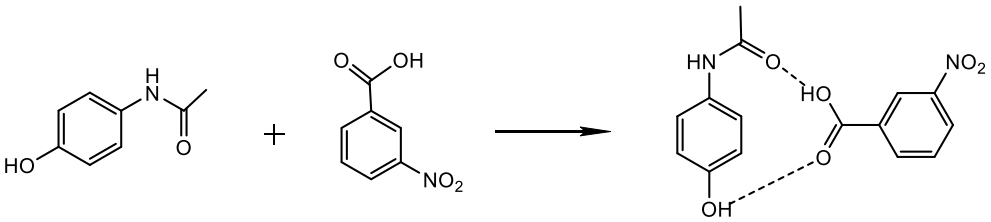

Fig. Co-crystal of Paracetamol and 3- NBA

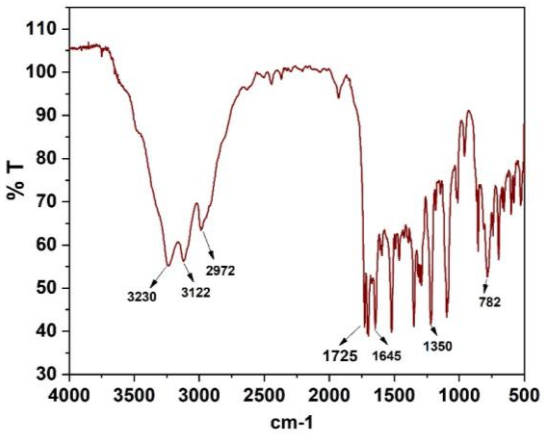

Fig. FTIR pattern for Paracetamol

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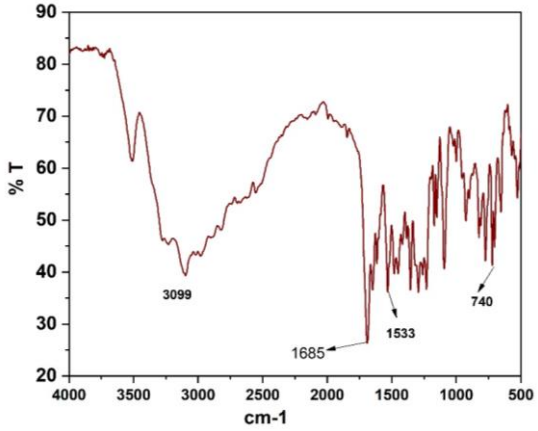

Fig. FTIR pattern for 3- Nitrobenzoic acid

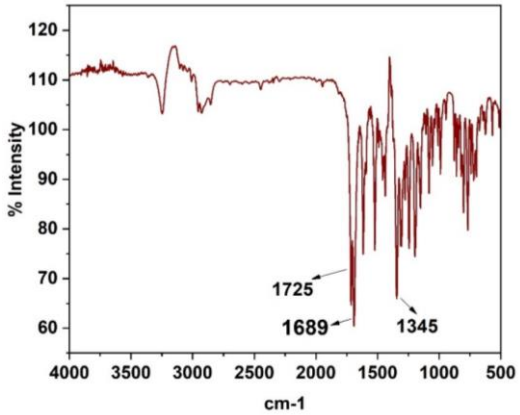

Fig. FTIR pattern for Paracetamol – 3-Nitrobenzoic acid (Mixture)

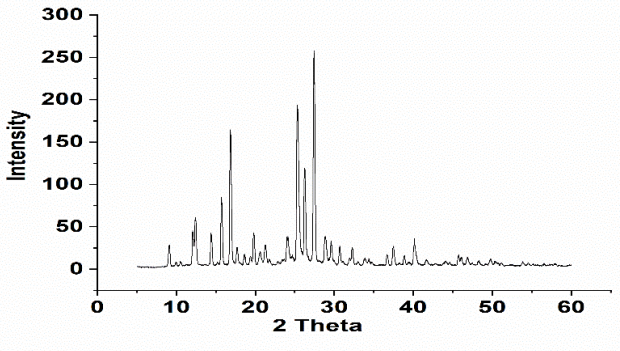

Fig. PXRD Pattern of Paracetamol

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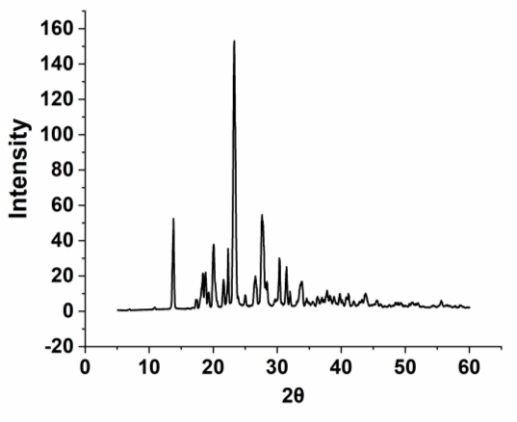

Fig. PXRD Pattern of 3-NBA

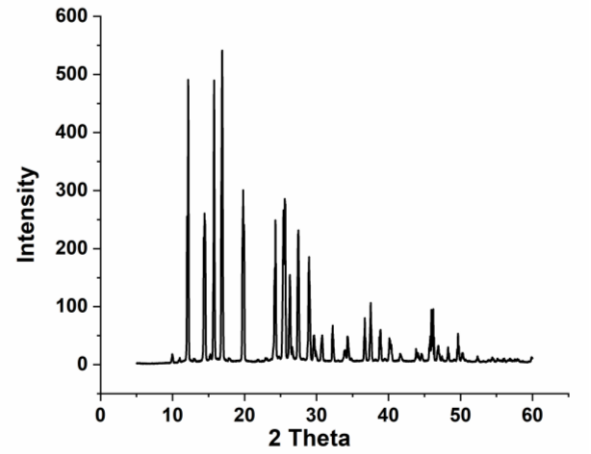

Fig. PXRD Pattern of Paracetamol – 3- NBA (Mixture)

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