

Current Research in **Chemistry**





∂ OPEN ACCESS

Current Research in Chemistry

ISSN 1996-5052 DOI: 10.3923/crc.2021.15.25



Research Article Optimization of Molecular Modeling and Spectroscopic Studies of 2-Acetoxybenzoic Acid with 2-Hydroxypropane-1,2,3-Tricarboxylic Acid Crystal

C. Muthuselvi, S. Amirthakani and M. Saranya

Department of Physics, Devanga Arts College, Aruppukottai-626101, Tamil Nadu, India

Abstract

Background and Objective: The commonly used drug of 2-acetoxybenzoic acid is used for the treatment of pain and fever due to various causes. The effect of drug may be increased if two compounds are taken together. Few studies have been encountered on investigation of drug-drug combination crystal. In this regard, the present research was carried out to perform the investigation of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal by theoretical and experimental methods. **Materials and Methods:** 2-acetoxybenzoic acid, 2-hydroxypropane-1,2,3-tricarboxylic acid, distilled water and ethanol are the raw materials used in the crystallization. The crystals were obtained by slow evaporation method at room temperature. **Results:** The grown crystal was characterized by powder XRD, FT-IR, Laser Raman, UV-Visible spectroscopy techniques and SEM with EDX analyzes. **Conclusion:** The computational study gives the optimized molecular structure with minimizing energy. Also, the crystal density was determined by the flotation method. The crystalline nature and average crystallite size has been performed using PXRD. The different functional groups present in the crystal were analyzed using IR and Raman spectroscopic techniques. The optical band gap was determined as 5.1 eV. The elemental composition was confirmed from the EDX study.

Key words: IR, raman, UV-Visible, MM2, AM1

Citation: Muthuselvi, C., S. Amirthakani and M. Saranya, 2021. Optimization of molecular modeling and spectroscopic studies of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal. Curr. Res. Chem., 13: 15-25.

Corresponding Author: C. Muthuselvi, Department of Physics, Devanga Arts College, Aruppukottai-626101, Tamil Nadu, India Tel: +919487672735

Copyright: © 2021 C. Muthuselvi *et al*. This is an open access article distributed under the terms of the creative commons attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

The 2-acetoxybenzoic acid is the chemical name of aspirin which is widely used as an anti-inflammatory and antipyretic drug^{1,2}. It is used to reduce the risk of heart attacks and strokes³. Also, it is used as a blood thinner, pain relief for mild aches, discomfort and to alleviate fever⁴. The 2-hydroxypropane-1,2,3-tricarboxylic acid (Citric acid) is a weak organic tricarboxylic acid that occurs naturally in citrus fruits⁵. It has two different hydrogen bonding functions specifically hydroxyl and acid groups⁶. The combination of aspirin and citric acid is used to relieve pain occurring together with heartburn and acid indigestion⁷. The discovery of new drugs is a difficult task and time consuming^{8,9}. However this problem is overcome by improving the formulations of existing drugs based on intermolecular interactions. This idea continues to enhance the pharmacological properties of drug compound with novel formulation¹⁰⁻¹². The Active Pharmaceutical Ingredient (API) incorporates with pharmaceutically-acceptable molecule without any structural modification of the parent drug in their crystal lattice. They are usually prepared by a variety of techniques such as recrystallization from solvents, melt crystallization and grinding etc which provides the alternate and interesting pathway to improve efficacy of a drug¹³⁻¹⁵. The drug-drug combination has the significant importance to reduce drug load and cost effects in the diagnosis of multiple diseases in recent years. Thus the development of combination drug shows the better effect than the sum of their individual effect particularly when all components are APIs. Therefore, the current study focused on the preparation of 2-acetoxybenzoic acid compound with 2-hydroxypropane-1,2,3-tricarboxylic acid single crystal and we have been successful in preparing this combination crystal by slow evaporation method and it was characterized using powder XRD, FT-IR, Laser Raman, UV-Visible spectroscopy techniques and morphology with elemental analyzes. The crystal structure was optimized by MM2 method using Chem 3D software.

MATERIALS AND METHODS

Study area: The crystal was grown in the month of November, 2020 at the Research Department of Physics, Devanga Arts College, Aruppukottai, Tamil nadu, India. Here all the data were collected from the various places in the month of December-January, 2021.

Chemical used: The 2-acetoxybenzoic acid, 2-hydroxypropane-1,2,3-tricarboxylic acid, distilled water and

ethanol were purchased from the Modern Scientific Company, Laboratory equipment supplier in Madurai, Tamil Nadu.

Methods: The 2-acetoxybenzoic acid compound with 2-hydroxypropane-1,2,3-tricarboxylic acid crystals were obtained by slow evaporation method at room temperature. The stoichiometric ratio (1:1) of 2-acetoxybenzoic acid and 2-hydroxypropane-1,2,3-tricarboxylic acid were dissolved with aqueous ethanol and stirred well using magnetic stirrer for 15 min. After the stirring process, the solution was filtered by filter paper and placed in the petridish. The mouth of the petridish was tightly covered by aluminum foil with small holes. After 30 days duration bulk color less crystals were formed by the slow evaporation process. The photographic view of grown crystal was shown in Fig. 1. The chemical structure of the 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal was depicted in Fig. 2.

Computational details: The optimized molecular parameters with the steric energy in (kcal mol⁻¹) were calculated using Molecular Mechanics (MM2) method in Chem3D program. The parameters obtained from this method were further optimized using a semi-empirical method Austin Model 1 (AM1) and the properties such as heat of formation, electronic energy and ionization potential were calculated. All the calculations were performed under gas phase conditions.

Characterization: The grown crystals were characterized by powder X-ray diffraction, FT-IR, Laser Raman and UV-Visible spectroscopic techniques, SEM with EDX and density measurement by flotation method.



Fig. 1: Grown crystal of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid



Fig. 2: Chemical scheme of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid

Powder XRD analysis: The crystalline quality of the grown crystals were studied by powder X-ray diffraction analysis using a XPERT-PRO X-ray diffractometer with Cu K α radiation (1.54060Å) in the 2 θ range 20°-80° at Alagappa University, Karaikudi.

Spectra data analysis: The FT-IR spectrum of title crystal was recorded using SHIMADZU FT-IR spectrometer in the range 400-4000 cm⁻¹ at V.H.N.S.N. College, Virudhunagar. The sample for this measurement was finally ground and mixed with KBr. The mixture was pressed under vacuum at very high pressure to obtain a transparent disc, which yield good spectra.

Laboratory spectral measurements were made with the Princeton Acton SP-2500 Raman spectrometer available in Alagappa University, Karaikudi. The source used in this device was the Nd: YAG laser operated at 514.5 nm with the incident power of 50-80 mW. The spectrum was recorded over a range of 500-3500 cm⁻¹. The sample was finely powered and pressed into a small depression in a metal disc and mounted on the sample compartment. This instrument has a resolution of 0.05 at 435.8 nm. The argon-neon laser at 435.8 nm was used as the excitation source of Raman measurement. A suitable notch filter was placed before the monochromatic to suppress the Rayleigh line.

The optical absorption spectrum of grown crystal has been recorded with SHIMADZU-UV 1601, double beam spectrometer at V.H.N.S.N. College, Virudhunagar. The absorbance data were observed for the title crystal in the wavelength range 190-1100 nm insteps of 1nm.The slit width chosen was 0.2 nm. The wavelength rate was in fast mode. The observed values of absorbance were recorded and stored in the memory of a computer and plotted.

SEM with EDX analysis: The CARLZEISS EVO18 scanning electron microscope was used to carry out the morphology

and elemental analysis which were collected from the Kalasalingam University, International Research Centre, Krishnankoil, Tamil Nadu, India.

RESULTS

The optimized molecular structure of the present compound using molecular mechanics MM2 calculation was represented in Fig. 3. The calculated optimized parameters were shown in Table 1. The total charge density surface map was shown in Fig. 4. The powder diffraction patterns of the (a) 2-acetoxybenzoic acid (b) 2-hydroxypropane-1,2,3tricarboxylic acid and (c) 2-acetoxybenzoic acid with 2hydroxypropane-1,2,3-tricarboxylic acid crystal was shown in Fig. 5. Determined values of crystallite size and dislocation density was represented in Table 2. The observed FT-IR and Laser Raman spectra were illustrated in Fig. 6 and 7, respectively. The observed wavenumber together with the assignments of the title compound were presented in Table 3. The UV-Visible absorbance spectrum and optical band gap graph was shown in Fig. 8 and 9 respectively. The morphology image and the EDX spectrum was exposing in Fig. 10 and 11.

DISCUSSION

The title crystal was grown by slow evaporation method and it was analyzed using powder XRD, IR, Raman, UV-Visible spectroscopy, SEM with EDX techniques and density measurement. These results were discussed and summarized in this present work. The optimized molecular structure was obtained using the Chem3D software.

Molecular modeling: The optimized molecular parameters of title compound were calculated using AM1 semi-empirical method in MOPAC that is available in Chem3D software. The



Fig. 3: Optimized molecular structure of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal with the atom-numbering. Hydrogen bonds are shown as dashed lines



Fig. 4: Total charge density surface map of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal

Optimized parameters	Calculated using MM2 and AM1methods	
Compound name	2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid	
Chemical formula	C ₁₅ H ₁₆ O ₁₁	
Molecular weight	372.28	
Final heat of formation	-470.87194 kcal	
Total energy	-5667.80659 eV	
lonization potential	10.19495	
Core-core repulsion	33678.07226 eV	
Steric energy	4.7020 kcal mol ⁻¹	

Table 1: Optimized molecular parameter data of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal





Fig. 5(a-c): Powder XRD diffraction patterns for (a) 2-acetoxybenzoic acid (b) 2-hydroxypropane-1,2,3-tricarboxylic acid and (c) 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal

Table 2: Determined values of crystallite size and dislocation density for 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal

Compound	Crystallite size (nm)	Dislocation density ($\times 10^{14} \text{ m}^2$)
2-acetoxybenzoic acid	42	5.67
2-hydroxypropane-1,2,3-tricarboxylic acid	40	6.25
2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid	58	2.97

calculated steric energy value using molecular mechanics method was also given in Table 1. The 2-acetoxybenzoic acid compound combine with 2-hydroxypropane-1,2,3-tricarboxylic acid through drug-receptor interactions by formation of O–H…O intermolecular interactions (Fig. 3). Drug-receptor interaction was displaced in Fig. 3. where the hydroxyl propane and carboxylic group of 2-hydroxypropane-1,2,3-tricarboxylic acid form hydrogen bond with carboxylic and ester group of 2-acetoxybenzoic acid. These hydrogen bonds optimize the stability of the complex crystal with steric energy 4.7020 kcal mol⁻¹. The total charge density was calculated by Huckel calculation and its charge density surface map was shown in Fig. 4.

Powder XRD analysis: The powder XRD diffraction patterns of pure2-acetoxybenzoic acid, pure 2-hydroxypropane-1,2,3-tricarboxylic acid and 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid combination crystals were compared in Fig. 5. Some additional peaks were appeared in the combination crystal which revealed that 2-hydroxypropane-1,2,3-tricarboxylic acid has entered into the

2-acetoxybenzoic acid lattice site. Also, the intensity of the combination crystal decreased when compared to parent crystal which suggests that combination crystal structure was distorted. The average crystallite size was determined using Debye-Scherrer formula and also the dislocation density can be calculated from the equation $\delta = 1/D^2 \text{ m}^2$. The powder X-ray diffraction peaks of parent crystals were indexed using INDX software. The crystalline size and dislocation density of both parent and combination crystals were compared in Table 2. The crystallite size was increased and dislocation density was decreased for the combination crystal.

Vibrational analysis: The 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid combination crystal has ester, carboxylic acid, disubstituted benzene ring and $-CH_2$ groups.

Ester group vibrations: The antisymmetric and symmetric stretching vibrations of $-CH_3$ group absorb close to 2960 and 2870 cm⁻¹, respectively¹⁶. The strong band at 2940 cm⁻¹ in Raman is attributed to antisymmetric $-CH_3$ stretching

Curr. Res. Chem., 13 (1): 15-25, 2021



Fig. 6: FT-IR spectrum of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal



Fig. 7: Laser raman spectrum of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal

vibration. The v_s (–CH₃) is observed as a strong band at 2870 cm⁻¹in IR spectrum only. The deformation antisymmetric and symmetric vibrational modes of –CH₃ group normally fall at 1465 and 1378 cm⁻¹, respectively¹⁷. In the present study, the bands identified at 1488 cm⁻¹ (IR) and at 1369 cm⁻¹ (IR), 1373 cm⁻¹ (Raman) spectra were assigned to the antisymmetric and symmetric deformation modes. The –CH₃ rocking vibrations appear in the range 922-919 cm⁻¹. The band for this mode was identified at 916 cm⁻¹ in the IR spectrum. The v (C=O) and v (C–O) vibrational modes occurs

between the region 1800-1770 and 1095-1016 cm⁻¹, respectively^{18,19}. For the title compound, the bands identified at 1850 and 1811 cm⁻¹ in IR spectrum was assigned to v (C=O) mode. The medium bands at 1092 and 1013 cm⁻¹ in the IR spectrum and at 1035 cm⁻¹ in Raman spectrum was attributed to the stretching mode of (C–O). For saturated esters, in general the O–C–C and C–C–O stretch falls in the 1100-1030 and 1210-1160 cm⁻¹ ranges¹⁹. For the title compound they are attributed at 1136 cm⁻¹ (IR) 1132 (Raman) and at 1188 cm⁻¹ (IR), 1182 cm⁻¹ (Raman).



Fig. 8: Absorbance spectrum for 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid c crystal



Fig. 9: Optical band gap for 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal

Carboxyl group vibrations: The characteristic C=O stretching of the carboxyl group appeared as a sharp peak between the 1725-1680 cm⁻¹ region²⁰. The strong absorption band at 1755 and 1690 cm⁻¹ were assigned to C=O stretching mode in the IR spectrum. These predictions agree well with the earlier studies^{20,21}. Aromatic acids have a strong band at 570-545 cm⁻¹ due to the rocking vibration of the CO₂ group. Also the bending vibrations of CO_2 group result in a band at 620-610 cm⁻¹ ²¹. In the present investigation, bands at 563 cm⁻¹ and 550 cm⁻¹ in IR and Raman spectra were assigned to CO_2 rocking vibration. The bending CO_2 group results in weak bands at 665 and 644 cm⁻¹ in IR and at 661 and 641 cm⁻¹ in Raman spectra. The C–O stretching of carboxylic acids appears near the region 1320-1210 cm⁻¹ in the spectra¹⁹.



Fig. 10(a-b): SEM images of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal with (a) 500X and (b) 1000X magnifications



Fig. 11: EDX spectrum of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal

In the present study, the C–O stretching of carboxylic acid was identified at 1306 and 1219 cm⁻¹ in the FT-IR spectrum. The carboxylic group exhibits a broad band between the region 3100-2800 cm⁻¹ for O–H stretching vibrations due to the presence of hydrogen bonding. The vibrations observed at 3082 cm⁻¹, 3019 cm⁻¹, 2870 cm⁻¹, 2833 cm⁻¹ in IR and at 3083 cm⁻¹ in Raman spectra were assigned to O–H stretching vibration of CO–OH group. The out-of-plane wagging mode of O–H group should be expected at 960-875 cm^{-1 20}. In the present case the bands observed at 970cm⁻¹ in IR and the band at 968 cm⁻¹ in Raman spectra were attributed to the O–H wagging

mode. The O–H twisting mode is expected to appear at 645, 598, 556 and 383 cm^{-1 21}. In the present work, bands at 644, 598, 563 and 542 cm⁻¹ in IR spectrum and bands at 641, 550 and 542 cm⁻¹ in Raman spectrum is allotted to t (O–H) mode. The wavenumber for the scissoring, wagging and rocking modes of O–C = O group are expected at 665, 577 and 502 cm⁻¹, respectively¹⁸. For the title crystal, the bands recognized at 665, 563 and 515 cm⁻¹ in FT-IR and at 641 and 550 cm⁻¹ in laser Raman spectra have been assigned to the scissoring, wagging and rocking modes of O–C=O group, respectively.

Table 3: Wavenumber assignments for 2-acetoxybenzoic acid with 2hydroxypropane-1,2,3-tricarboxylic acid crystal in FT-IR and Laser-Raman spectra

Nainan	эресна	
FT-IR (ū/cm ⁻¹)	Laser-raman (ū/cm ⁻¹)	Assignment
3082 (s, br)	3083 (s)	v (O–H); v (C–H)
3019 (s, br)	-	ν (O–H); ν (C–H)
-	2940 (s)	v_{as} (-CH ₂)
2918 (sh)	-	v_{as} (-CH ₂)
2870 (s, br)	-	ν _s (–CH ₃), ν (O–H)
2833 (s)	-	ν (O–H), ν _s (–CH ₂)
1850 (w)	-	v (C=O) _{ester}
1811 (sh)	-	v (C=O) _{ester}
1755 (s)	-	v (C=O) _{acid}
1690 (s)	-	v (C=O) _{acid}
1605 (m)	1604 (s)	ν (C=C)
1576 (w)	-	v (C–C)
1524 (w)	-	v (C–C)
1488 (s)	-	δ_{as} (–CH ₃)
1458 (m)	-	ρ (–CH ₂)
1369 (m)	1373 (w)	δ _s (-CH ₃), ω (-CH ₂)
1306 (m)	1292 (m)	v (C–O) _{acid}
-	1274 (m)	ν (C–O) _{acid} , β (C–H)
1219 (m)	-	ν (C–O) _{acid} , β (C–H), t (–CH ₂)
1188 (s)	1182 (m)	ν (C–C–O), β (C–H)
1136 (m)	1132 (w)	ν (O–C–C), β (C–H)
1092 (m)	-	ν (C–O) _{ester} β (C–H)
1038 (m)	1035 (m)	β (C–H), Benzene ring
		breathing mode
1013 (m)	-	ν (C–O) _{ester} , β (C–H)
970 (m)	968 (w)	ω (O–H)
916 (s)	-	τ (–CH ₃) , γ (C–H)
880 (sh)	-	γ (C–H)
839 (w)	-	γ (C–H)
800 (w)	782(m)	γ (C–H)
754 (w)	743(m)	γ (C–H)
704 (w)	712 (m)	γ (C–H)
665 (w)	661(m)	δ (CO ₂), ρ (O–C=O), γ (C–H)
644 (w)	641(m)	δ (CO ₂), t (O–H), γ (C–H)
598 (w)	-	t (O–H)
563 (w)	550 (m)	τ (CO ₂), t (O–H), ω (O–C=O)
542 (w)	542 (m)	t (O–H)
515 (w)	-	τ (O–C=O)

w: Weak, s: Strong, m: Medium, sh: Shoulder, v: Stretching, v_s: Symmetric stretching, v_{as}: Anti symmetric stretching, δ : Bending, δ_s : Symmetric bending, δ_{as} : Antisymmetric bending, γ : Out of plane bending, β : In plane bending, ρ : Scissoring, t: Twisting, ω : Wagging and τ : Rocking

Disubstituted benzene ring vibrations: For the ortho substituted benzene ring, the C–H vibration generally appears in the region 3120-3000 cm⁻¹²². The bands observed at 3082 and 3019 cm⁻¹ in FT-IR and at 3083 cm⁻¹ in Raman spectra was assigned to C–H stretching vibrations. The C–H in-plane bending vibrations produce the bands between the region 1300-1000 cm^{-1 23}. The vibration bands appeared at 1219, 1188, 1136, 1092, 1038 and 1013 cm⁻¹ in IR spectrum and at 1274, 1182 and 1035 cm⁻¹ in Raman spectrum were attributed to the β (C–H) mode. Aromatic C–H out-of-plane bending vibrations usually occurs in the range 960-690 cm⁻¹. The bands noticed at 916, 880, 839, 800, 754, 704, 665 and

641 cm⁻¹ (Raman) were designate to γ (C–H) mode. In FT-IR spectrum, the observed the bands at 1605 and 1576 cm⁻¹ were appoint to C=C and C–C stretching vibrations. The ring breathing mode for ortho substituted benzene ring is normally observed at 1040 cm⁻¹ ^{22,23}. The appearance of medium absorption bands at 1038 cm⁻¹ in IR and 1035 cm⁻¹ in Raman was recognized the ring breathing mode for the title compound.

644 cm⁻¹ (IR) and at 782 cm⁻¹, 743 cm⁻¹, 712 cm⁻¹, 661 cm⁻¹,

Vibrations–CH₂ group: The antisymmetric and symmetric stretching vibrations of $-CH_2$ group appear in the region 2925±10 and 2855±10 cm⁻¹, respectively²⁴. The scissoring, wagging and twisting vibrations of $-CH_2$ group were observed in the region 1463±10 and 1390-1180cm^{-1 25}. The v_{as} ($-CH_2$) mode was assigned at 2918 cm⁻¹ in Raman spectrum and v_s($-CH_2$) was attributed at 2833cm⁻¹ in IR spectrum for the title compound. The bands observed at 1458, 1369 and 1219 cm⁻¹ (IR) and at 1373 cm⁻¹ (Raman) were assigned to the scissoring, wagging and twisting modes of $-CH_2$ group.

UV-Visible spectroscopy analysis: The high transparency was confirmed from the recorded spectra and observed that there was no significant absorption in the range 383-1100 nm which leads to wide transparency range in the visible region. The lower cut-off wavelength was found to be at 254, 293 and 383 nm. The title crystal has the maximum absorbance peaks at 274 and 351 nm.

Determination of optical band gap: The plot of variation of $(\alpha hv)^2$ Vs photon energy (hv) was shown in Fig. 9. The plot is known as Tauc's plot and it is used to find out the accurate optical band gap value. The optical band gap was evaluated by the extrapolation of the linear part of $(\alpha hv)^2$ to the photon energy axis and the value was found to be as 5.1 eV. As a consequence of wide band gap the grown crystal has large transmittance in the visible region.

SEM with EDX analysis: This technique was used to analyze surface morphology and elemental composition of title compound. SEM images were taken with 500x and 1000x magnifications with acceleration voltage of 22 kV which was depicted in Fig. 10. The structural morphology consists of ocean wave like shape. The EDX band spectrum of title crystal was shown in Fig. 11. The atomic percentage of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid crystal was found to be as 88.45% for C and 14.49% for O elements.

Crystal density analysis: The density of crystal was determined by the flotation method. The sample is crushed to comparable size and is placed in a small test tube containing bromoform. The sample will float on the liquid surface indicating that the density of the liquid is greater than that of the sample. The less dense liquid, xylene is then added slowly, drop wise with stirring until the particle is exactly suspended. One should be careful while adding the mixture that it should be stirred with each addition so that air bubbles, if any are removed. If the sample particles remain suspended in the liquid, then their densities are equal to each other and to that of the liquid mixture. Particles with different densities will either sink or float depending upon whether they are denser or less dense than the liquid medium. Now, density of the crystal is calculated by using the Eq:

$$D = \frac{W 3 - W 1}{W 2 - W 1} g/cc$$

where, W1 is the weight of the empty specific gravity bottle, W2 is the weight of the specific gravity bottle with water and W3 is the weight of the specific gravity bottle with solution.

The determined density values of parent crystal are 1.40 (g/cc)for 2-acetoxybenzoic acid, 1.67 g/cc for 2-hydroxypropane-1,2,3-tricarboxylic acid and 1.28 g/cc for the combination crystal. The density value of combination crystal lies between their parent substances. This shows that the grown crystal is a complex one.

CONCLUSION

Using the slow evaporation method, the combination crystal of 2-acetoxybenzoic acid with 2-hydroxypropane-1,2,3-tricarboxylic acid have been crystallized successfully at room temperature. The minimized energy structure has been performed by Chem3D software. The INDX software was used to index the diffraction peaks of parent compounds. For the combination crystal, the crystallite size was increased and also dislocation density was decreased. The wavenumber assignments for various functional groups were executed using spectroscopic techniques and all the wavenumber values were in good agreement with already reported literature values. Due to the wide optical band gap, the title crystal has the high transparency in the visible region. The surface morphology was also studied by SEM analysis and the results indicate the compound has ocean wave like morphology. The density of combination crystal was determined as 1.28 g/cc by the flotation method.

SIGNIFICANCE STATEMENT

This study realizes the combination of drugs that can be play the widespread roles in the pharmaceutical field. This study will help the researcher to discover the new drug compound. In order to improve the effect of drug properties, an attempt was made on the preparation of combination drug crystal by slow evaporation method.

ACKNOWLEDGMENT

The authors sincerely acknowledge their gratitude to the Management and Principal of Devanga Arts College, Aruppukottai for their consent and support during their research work.

REFERENCES

- 1. Ayyadevara, S., P. Bharill, A. Dandapat, C. Hu and M. Khaidakov *et al.*, 2013. Aspirin inhibits oxidant stress, reduces age-associated functional declines and extends lifespan of caenorhabditis elegans. Antioxid. Redox Signaling, 18: 481-490.
- Parvez, M.M., H.J. Shin, J.A. Jung and J.G. Shin, 2017. Evaluation of para-aminosalicylic acid as a substrate of multiple solute carrier uptake transporters and possible drug interactions with nonsteroidal anti-inflammatory drugs *in vitro*. Antimicrob. Agents Chemother., Vol. 61, No. 5. 10.1128/AAC.02392-16.
- Wang, C., C. Wang, Q. Liu, Q. Meng and J. Cang *et al.*, 2014. Aspirin and probenecid inhibit organic anion transporter 3-mediated renal uptake of cilostazol and probenecid induces metabolism of cilostazol in the rat. Drug Metab. Dispos., 42: 996-1007.
- 4. Brazier, Y., 2020. Uses, benefits and risks of aspirin. https://www.medicalnewstoday.com/articles/161255#prec autions.
- Abdel-Salam, O.M.E., E.R. Youness, N.A. Mohammed, S.M.Y. Morsy, E.A. Omara and A.A. Sleem, 2014. Citric acid effects on brain and liver oxidative stress in lipopolysaccharide-treated mice. J. Med. Food, 17: 588-598.
- Gailus, T., H. Krah, V. Kühnel, A. Rupprecht and U. Kaatze, 2018. Carboxylic acids in aqueous solutions: Hydrogen bonds, hydrophobic effects, concentration fluctuations, ionization and catalysis. J. Chem. Phys., Vol. 149. 10.1063/1.5063877.
- 7. Drugs.com, 2020. Aspirin, sodium bicarbonate and citric acid (oral). https://www.drugs.com/cons/aspirin-sodium-bicarbonate-and-citric-acid.html.

- Chen, J., X. Luo, H. Qiu, V. Mackey, L. Sun and X. Ouyang, 2018. Drug discovery and drug marketing with the critical roles of modern administration. Am. J. Transl. Res., 10: 4302-4312.
- 9. Löscher, W., H. Klitgaard, R.E. Twyman and D. Schmidt, 2013. New avenues for anti-epileptic drug discovery and development. Nat. Rev. Drug Discovery, 12: 757-776.
- Bergström, C.A.S., W.N. Charman and C.J.H. Porter, 2016. Computational prediction of formulation strategies for beyond-rule-of-5 compounds. Adv. Drug Delivery Rev., 101: 6-21.
- Thakuria, R. and B. Sarma, 2018. Drug-drug and drug-nutraceutical cocrystal/salt as alternative medicine for combination therapy: A crystal engineering approach. Crystals, Vol. 8. 10.3390/cryst8020101.
- 12. Saikia, B., P. Bora, R. Khatioda and B. Sarma, 2015. Hydrogen bond synthons in the interplay of solubility and membrane permeability/diffusion in variable stoichiometry drug cocrystals. Crystal Growth Des., 15: 5593-5603.
- Thakuria, R., A. Delori, W. Jones, M.P. Lipert, L. Roy and N. Rodríguez-Hornedo, 2013. Pharmaceutical cocrystals and poorly soluble drugs. Int. J. Pharm., 453: 101-125.
- 14. Trask, A.V., W.D.S. Motherwell and W. Jones, 2005. Pharmaceutical cocrystallization: Engineering a remedy for caffeine hydration. Crystal Growth Des., 5: 1013-1021.
- 15. Pourkavoos, N., 2012. Unique risks, benefits and challenges of developing drug-drug combination products in a pharmaceutical industrial setting. Combination Prod. Ther., Vol. 2. 10.1007/s13556-012-0002-2.
- Gipson, K., K. Stevens, P. Brown and J. Ballato, 2015. Infrared spectroscopic characterization of photoluminescent polymer nanocomposites. J. Spectrosc., Vol. 2015. 10.1155/2015/489162.

- Boczar, M., M.J. Wójcik, K. Szczeponek, D. Jamróz, A. Zięba and B. Kawałek, 2003. Theoretical modeling of infrared spectra of aspirin and its deuterated derivative. Chem. Phys., 286:63-79.
- Pazos, I.M., A. Ghosh, M.J. Tucker and F. Gai, 2014. Ester carbonyl vibration as a sensitive probe of protein local electric field. Angew. Chem. Int. Ed., 53: 6080-6084.
- 19. Yu, Y. and L. Shi, 2019. Vibrational solvatochromism of the ester carbonyl vibration of pcbm in organic solutions. J. Chem. Phys., Vol. 151. 10.1063/1.5111046.
- Nandi, C.K., M.K. Hazra and T. Chakraborty, 2005. Vibrational coupling in carboxylic acid dimers. J. Chem. Phys., Vol. 123. 10.1063/1.2039084.
- 21. Muthuselvi, C., A. Arunkumar and G. Rajaperumal, 2016. Growth and characterization of oxalic acid doped with tryptophan crystal for antimicrobial activity. Der Chem. Sin., 7: 55-62.
- 22. Smith, B.C., 2016. Distinguishing structural isomers: Mono- and disubstituted benzene rings. Spectroscopy, 31: 36-39.
- 23. Muthuselvi, C., S.S. Pandiarajan, B. Ravikumar, S. Athimoolam and R.V. Krishnakumar, 2018. Halogen substituted indeno quinoxaline derivative crystal: A spectroscopic approach. Asian J. Applied Sci., 11: 29-37.
- Sheela, G.E., D. Manimaran, I.H. Joe and V.B. Jothy, 2017. Studies on molecular structure and vibrational spectra of NLO crystal L-glutamine oxalate by DFT method. Indian J. Sci. Technol., 10: 1-23.
- Pawlukojć, A., K. Hołderna-Natkaniec, G. Bator and I. Natkaniec, 2014. L-glutamine: Dynamical properties investigation by means of INS, IR, RAMAN, ¹H NMR and DFT techniques. Chem. Phys., 443: 17-25.