REVIEW OF SPECTROSCOPIC INVESTIGATION ON FUNDAMENTAL MODES OF DFT STUDIES IBUPROFEN SUBSTITUTED DRUG ANALYSIS..

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Abstract

In a previous communication we reported on the synthesis of Ibuprofen sodium representatives of the category of compounds possessing sort of biological activities. The computation method of Ibuprofen sodium tablet this study aimed to determination of physical properties like appearance solubility, freezing point . The elucidation of the trail of the reaction and therefore the study of its scope and artificial applications bring back need the further spectral investigation are confirmed from FT-IR, H1NMR, C13 NMR. The UV absorption was administered which shows the cutoff wavelength around 520 nm. Fourier transform infrared (FT IR) spectral analysis was wont to confirm the presence of varied functional groups within the structure. Frequency doubling is exhibited by Ibuprofen sodium single crystals and their NLO was better than of KDP. The high SHG efficiency that Ibuprofen sodium has the very best potential as a candidate material for NLO applications

INTRODUCTION

Ibuprofen the first member of this group to come into general use has been 2. 4-isobutyl phenyl propionic acid. It forms white or almost white powder or crystals. . It as characteristic odour. . It is insoluble in water. It is soluble in organic solvent like Ethanol and Acetone. Ibuprofen has been not recommended for use by pregnant women. • It should be kept in well closed containers at room temperature. Isobutyl phenyl propionic acid is associated with several suspected or probable interaction that can affect the action of other drugs.Chemical industry zone with common effluent-discharge facility, innovative plant layout and high degree of mechanization. It has a separate multi-utility plant capable of undertaking custom manufacturing of Nizatidine from pilot plant to commercial scale achieved in record time. Modern laboratory with comprehensive facilities including microbiological testing, modern fire hydrant and fire alarm system spread over 44,000 square meter and ultra modern packing section and state of the

drying equipments are salient features of plant. Pharmaceutical chemistry is a study of compounds used in medicine, embracing the main branches of chemistry like analytical chemistry, physical and organic chemistry. Medicinal chemistry is concerned with the isolation determination of structure and synthesis of compounds, which are used in medicines. It involves the study of the metabolism and mechanism of action of drugs and the relationship between structure and biological activity. In the past few decades there has been a hiatus in the momentum of research and discover of “novel” medical compounds. The word drug is derived from the French word "drogne". which mean "herb”.

The source of drugs is chemical analysis, Micro organisms, Minerals, Higher flowering plants and animals. The synthetic drugs are obtained by modification of the structure of naturally occurring drugs or by pure synthesis. It is possible to prepare to prepare many new analgesics, anesthetics, antipyretics, anti inflammatory etc., by chemical

Analgesics are group of drugs which relief pain they act on the central nerve system and causes in sensibility to pain they are generally classified as

1. Narcotics analgesics. 2. Non Narcotics analgesics.

Ibuprofen may increase the blood level of lithium by reducing the excretion of lithium by the kidneys. Increased level of lithium may lead to lithium toxicity. Ibuprofen may be used in combination with amino glycosides the blood levels of the aminoglycosides may increase; presumably the elimination of amino glycoside from the body is reduced. It is used as Non steroidal anti inflammatory, 2. It is used as analgesics. 3. It is used as antipyretics. Ibuprofen (from the now outdated nomenclature iso-butyl-propanoicphenolic acid) is a non-sterodial anti-inflammatory drug (NSAID) originally marketed as brufen and since then under various other trademarks most notably nurofen, Advil and mortin. It is uses for relief of symptoms of arthritis, primary dysmenorrheal, fever, and as an analgesic, especially where there is an inflammatory component. Ibuprofen is known to have an antiplatelet effect, though it is relatively mild and short-lived when compared with that of aspirin or other more well-known antiplatelet drugs. Ibuprofen is a core medicine in the the world health organization's "Essential drugs list", which is a list minimum medical needs for a basic health care system.

STRUCTURE OF IBUPROFEN SODIUM

sodium2-[4-(2methyl-propyl) phenylpropanoate

Na -

Experimental Methods

The 1H & 13C NMR spectra were recorded on a BRUKER 400 MHz NMR spectrometer using DMSO as solvent. the space temperature Fourier transform infrared spectra of Ibuprofen sodium were recorded within the range 400-4000 cm-1 at a resolution of ±5 cm-1 employing a BRUKER spectrophotometer equipped with a LiTaO3 detector, a KBr beam splitter, a He-Ne laser source and a boxcar atomization used for 250 averaged interferograms collected for both the sample and therefore the background. High performance liquid chromatography. an appropriate HPLC instrument equipped with UV detector. Column using Themoquest Hypersil ODS 150 X 4.6mm, 5µm (or) equivalent. The quantum chemical computations of this heterodimer were employed with density functional theory (DFT) method by using Gaussian 09 [11] program package with basis set of 6-311++G (d,p). The SCXRD crystallographic information file (CIF) file of ibuprofenwas used as an input. The optimized structure of this crystal was visualized using Chemcraft v1.8 software [13]. the very best occupied molecular orbital (HOMO), lowest unoccupied

molecular orbital (LUMO), Molecular electrostatic potential (MEP) and hyperpolarizability of the isolated molecule were calculated from an equivalent basis set. the entire charge spread is described by MEP. HOMO-LUMO energy gap affirms the chemical softness of the fabric . of these parameters were visualized using Gaussview software

CHEMICAL NAMES:

Acetone, Ethanol, Potassium bromide, Sodium hydroxide, Phosphoric acid, Acetonitrile, Propanol, Thioacetamide, perchloric acid, Potassium permanganate sulphuric acid

(Impurity J) [2-(4-Isobutyryl phenyl) propanoic acid

(Impurity -A) 2-[3-(2methyl propyl) phenyl] propanoic acid

Result and discussions

ANALYSIS OF IBUPROFEN SODIUM:

RESIDUAL SOLVENTS:

Preparation of internal standard working.

Solution (ISTD WS):

Weighed 50.6mg of n-propanol in a 500ml volumetric flask containing 100ml of water mixed and made upto 500ml with water.

Standard preparation:

Stock solution:

Weighed 100.4mg of Toluene in a 100ml volumetric flask containing 50ml

of ISTD WS and made upto 100 ml with ISTD WS from that 10ml of

solution pipetted out into a 100ml volumetric flask and made up to the

volume with ISTD WS.

Standard working solution:

Pipetted out 5ml from of stock solution in a head space sample vial and crimped properly using crimper and placed 6 numbers of vials.

SYSTEM SUITABILITY:

RUN NO

SOLVENT RATIO TOLUENE

AVERAGE 1.8186 % RSD

4.0

SYSTEM SUITABILITY: Passes

phenyl] propanoic acid LT 0.03% (Impurity D)

2-[4-hydroxy-2-methyl propyl]phenyl) propanic LT 0.03% acid (Impurity L)

2 RS-2-hydroxy-2-[4-(2

methyl propyl)-phenyl) LT 0.03% unspecified propanoic acid (Impurity M)

Any impurity, RRT 0.60, Total impurities 0.04%

OPTICAL ROTATION:

Preparation of 0.1N NaOH:

Sample solution:

Weighed 2.50050g of Ibuprofen sodium in 100ml of volumetric flask dissolved and diluted to the volume with 0. IN NaOH

NON-STEROIDAL ANTI-INFLAMMATORY:

The drugs which are used to diminish or reduce inflammation and the pain arising from it are termed as anti inflammatory agents.

ANTIPYRETICS:

Those drugs which are used t bring down the body temperature during high

fever.

Ibuprofen:

They are known to have much lower maximal effects than do the opioid analgesics which find use for the relief of more serve type of pain.

These drugs can be classified as

1. Salicylic acid derivatives. 2. Aryl acetic acid derivatives. 3. Pyrazole derivatives. 4. N-arylanthranilic derivatives.

Ibuprofen is classified under the aryl acetic and derivatives.

Ibuprofen has been the drug of the class where in addition to an aryl substituent on a carbon of acetic and there is a methyl group attached to it.

These many appropriately be termed as propionic acid derivatives

INFRARED SPECTROSCOPY:

Region in cm and intensity	Stretching
3350	N-H str
3000-3100	c≡c-H str
3080	C-H (aromatic)
1710	C=O str
1680-1650	N=O str
2960-2850	C-H str
1020-1070	C=C – O –C
1500-1570	Ar – NO2
1620-1535	-N=0
~3500	N-H str (1°amine, amide)
~3400	N-H str (1°amine, amides) H-bond

Compare the spectrum with the reference spectrum. The sample spectrum exhibits maxima only at the utmost wave length that of reference spectrum. After analysis remove the pellet holder from the compartment discard the pellet.

IR ABSORPTION SPECTRUM:

Sample Preparation:

Fourier transform infrared analysis of Ibuprofen sodium compound carried out using KBr pellet technique in the wave length between 4000 and 400 cm^{-1} and the recorded IR spectra are shown in the below table. The wave-numbers of the peaks and their assignment are given Ibuprofen in dentification of infrared spectroscopy. The IR range is identified peaks in 1702 are **thanks to** c=o stretching (Ketone). From the position of absorption bands shows a band at 3348.76 in N-H stretching, 290 in C-H stretching, 1275.41 is (N=O) nitro compounds, 3080 is C-H stretching is aromatic ring and 1055.17 is C=C-O-C stretching. Absorption position of 602, 622.08, 670.11, and 696.84 is C-H def. There absorption at 2991.84 is C-H stretching.

Region in cm^{-1} and intensity	**Absorption**
1702	C=O str (Ketone)
3348.76	N-H str
2940	C-H str
1275.41	-N=0 str
3080	C-H str (Aromatic ring)
1055.17	C=C-O-C
670.11, 696.84	C-H def
2991.84	C-H str in CH_3

Melting Point:

Ensure that the sample is within the sort of fine powder, if not crush the sample to a fine powder. Fill sample during a meeting point capillary , to approximately 2mm height top it and insert it into the sample hole provides on the highest of the instrument. Observe through view glass the beginning of meeting. The lower display show the initial temperature press ‘stop’ at the top of the meeting. Now upper display shows the ultimate temperature write the initial and final temperatures. Stop the heater. Carefully

remove the capillary from the part and permit the oil bath to chill right down to temperature.

LOSS ON DRYING:

Accurately weighted a clean previously dried(for half-hour) and cooled LOD bottle(W1) Mix and weigh accurately about 1gm of sample with the LOD bottle(W2).Place the loaded LOD bottle within the drying chamber. Dry the sample at the temperature 105degree c for 4 hours. Take the LOD bottle and keep it inside the desiccators. Allow it to achieve the space temperature and weigh(W3).Continue the drying until constant weight is obtained. Until two consecutive weighing don't differ by quite 0.50mg per gram of substance taken, the second weighing following a further hour of drying.

Calculation:

$$\text{Loss on drying (\%W/W)} = \frac{Loss\ of\ weig\ ht\ (W2-W3)}{weig\ ht\ of\ sample\ (W2-W1)} \times 100$$

Where,

W1- Empty weight of the LOD Bottle with lid.

W2- Weight of the LOD bottle with lid and sample before drying.

W3- Weight of the LOD bottle with lid and sample after drying.

RESIDUAL IGNITION (sulphated Ash)

Weigh accurately about 1gm of the sample into a previously cleaned, ignited, and cooled and weighed a platinum/silica crucible. Moisten the sample with vitriol , and keep the crucible within the electric bunsen and ignite gently until the sample get charged continue ignition till no fumes are evolved. Transfer the crucible into muffle furnace. Ignite it at 600+- 50 °c until the carbon is consumed. Allow the crucible to chill to temperature and weigh continue the ignition until constant weight is obtained.

Until two consecutitive weighing don't differ by quite 0.50mg per gram of substance taken the second weighing following a further 15 to half-hour ignition period.

Calculations:

Residue on ignition (%W/W) = $\frac{weig\ ht\ of\ the\ residue\ (in\ g)}{weig\ ht\ of\ the\ sample\ (in\ g)} \times 100$

UV-visible-NIR spectral studies

The optical transmission were recorded from UV-Vis- IR in the wavelength range of 200-2500 nm^{-1}. Figure.4. shows that the optical transmission spectrum of grown crystal in which characteristic transmission of Ibuprofen sodium crystal occurs 230 nm. Bandgap energy is calculated at 3.0 ev and the transparency percentages are 70.94%, which makes them potential candidates for second harmonic generation (SHG) applications. The absorption coefficient was calculated at different location of the grown crystal. The good transmittance property of the crystal in entire visible region clearly indicates that the grown crystals can be used for NLO application. The diffuse reflectance spectra were translated into the absorption spectra by the Kubelka-Munk method. Kubelka-Munk's equation is described as follows:

$$\alpha = (1-R)^2/2R \text{ ----- (1)},$$

'α' where is the absorption coefficient and 'R' the reflectivity at a particular wavelength. The band gap energy can be determined using the Tauc relation. According to the Tauc relation, the absorption coefficient 'α' for a material is given by

$$\alpha h\nu = A(h\nu - E_g)^n \text{-- (2)},$$

Where E_g the band gap, constant A is different for different transitions, *h* is the Planck's constant and 'ν' the frequency of the incident photons. (hν) is energy of photon in eV and n denotes the nature of the sample transition. The 'n' in the equation has values 1/2, 2, 3/2 and 3 for allowed direct, allowed indirect, forbidden direct and forbidden indirect transitions [10-11] respectively. The TAUC plot of a sample defines the optical band gap as the region A in fig.5. The tauc plot of the sample is given in Fig 5. The band gap of NMNPB crystal was estimated by plotting $(\alpha h\nu)^{1/2}$ versus $h\nu$ as shown in Fig. 5 and extrapolating the linear portion near the onset of absorption edge to the energy axis. From Fig. 5, value of band gap is obtained as 3.0 eV. It is reported that optical gap energy of nano –sized crystal depends on its crystallite size, [12-15].

Proton NMR spectral analysis

Nuclear magnetic resonance (NMR) spectral analysis is an important analytical technique used to determine the structures of organic compounds. Fig.6. shows that the proton NMR spectra of the molecule Ibuprofen sodium, exhibits a three singlet peaks were 2.44 ppm (S, 3H, CH3), 7.83 ppm (S, 3H, CH) due to the presence of methyl group. Two doublet peaks were observed at 7.24 ppm (d, 2H, ArH), 7.05 ppm (d, 2H, ArH) due to the presence of aromatic protons of acetate. Doublet of doublets were observed at 7.95 & 7.97 ppm (dd, 2H,ortho & meta) in aromatic compounds. Two triplet peaks were observed at 7.61 (t, 3H, ArH) & 7.53 ppm (t,3H, ArH) in aromatic ring.

^{13}C NMR spectral analysis

Figure shows the ^{13}C NMR spectra of Ibuprofen sodium show a . This carbon signals at 176.66 ppm in the downfield respectively due to the highly deshielded carbonyl carbon of the benzamide moiety. The peaks due to aromatic carbons appears at 117.82, 119.87, 127.11, 126.07, 130.05, 134.49, 135.06, 138.64, 176.23, and 146.95 ppm in the case of Ibuprofen sodium. The peak at 18.20 ppm in the upfield region is due to methyl carbon.

Powder X-ray diffraction studies

Powder X-ray diffraction (XRD) is a powerful tool in identifying different crystal phases by their unique diffraction patterns [16]. As-grown Ibuprofen sodium crystals were finely powdered and subjected to powder XRD analysis at room temperature. The sample was scanned over the range of 10 to 90 degree at a scan rate of 0.02°/minute. All the observed reflection lines were indexed with the help of computer program WinPLOTR as shown in Fig.8. The well-defined Bragg peaks are sharp, confirming good crystallinity of all the grown crystals.

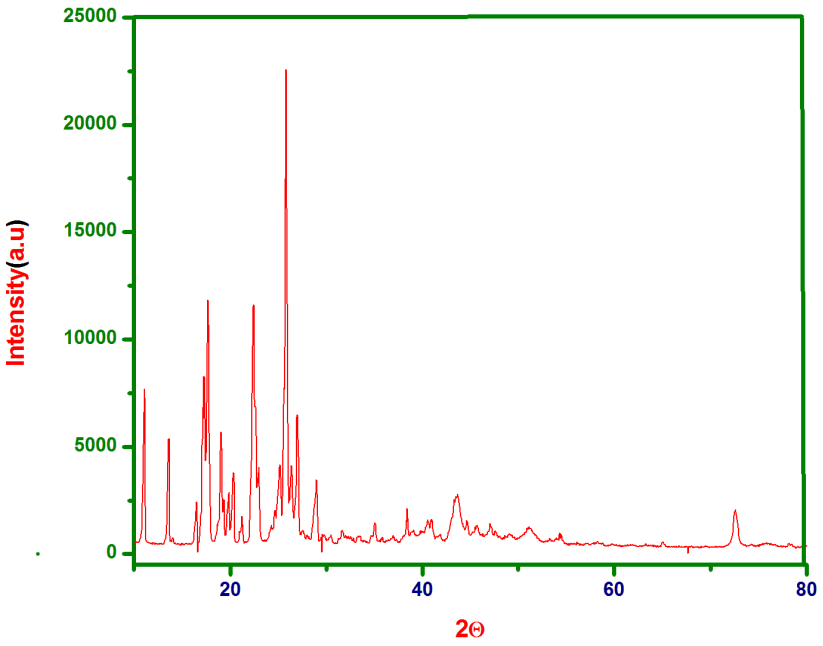

Fig. 8. Powder X-ray diffraction patterns of Ibuprofen sodium

Powder SHG studies

The second harmonic generation (SHG) activity of the grown crystal was examined by Kurtz and Perry technique [17]. It is an important tool to evaluate the conversion efficiency of NLO materials. The NMNPB single crystals were ground to powder and
packed between two transparent glass slides. The first harmonic output of 1064 nm from a Nd:YAG laser was made to fall normally on the prepared sample with pulse width of 10 ns. It was found that frequency doubling occurs in Ibuprofen sodium crystals. NLO efficiency of these crystals is better than that of KDP and the values are compared in Table 3. The level of NLO response of a given material is inherently dependent upon its structural attribute. On a molecular scale, greater the extent of charge transfer across the material larger is the NLO output. The laser damage threshold of Ibuprofen sodium are found to be much higher than that of KDP and these values are presented in Table 3. This study indicates that structural bonding level owing to their electrostatic and directed nature. From the above observations the grown crystals such as Ibuprofen sodium the SHG efficiency was higher than that of KDP. Among the crystals studied, Ibuprofen sodium shows the highest SHG efficiency and it is 2.02 times greater than that of KDP crystal. This concludes that this crystal is a potential candidate for NLO applications.[18]

CONCLUSION:

Ibuprofen sodium is a derivative of Ibuprofen substance which used as analgesic. Some important analytical parameter such as widely used as a melting point, moisture content, assay, loss on drying were carried out in determine the purity of raw materials used for the production of Ibuprofen sodium. All the analytical parameters determined correlated with the theoretical and standard values. The dominant peaks in the IR spectra of Ibuprofen are correlated with observed value and theoretical value. The results are suitably interperated. The purity of the 600mg Ibuprofen sodium tablet (99%) is confirmed by assay test UV spectra, H^1 NMR, C^{13} NMR. From these methods it is concluded that the purity of the tablet is 99.8%. If impurities present in the tablet it will produce some side effects. Frequency doubling is exhibited by Ibuprofen sodium single crystals and their NLO was better than of KDP. The high SHG efficiency that Ibuprofen sodium has the highest potential as a candidate material for NLO applications.

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