ORIGINAL RESEARCH ARTICLES

SYNTHESIS, STRUCTURAL CHARACTERIZATION AND SOLUBILITY INVESTIGATION OF FLURBIPROFEN ISOBUTANOL AMMONIUM SALT

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ABSTRACT

This research is centered on the conversion of active pharmaceutical ingredients (APIs) into salt formulations, aiming to enhance their solubility, improve absorption into the bloodstream, and ultimately elevate their therapeutic effectiveness. More specifically, it delves into the synthesis and detailed characterization of flurbiprofen isobutanol ammonium salt. The confirmation of salt formation was achieved through a comprehensive analytical approach, including differential scanning calorimetry (DSC), thermogravimetry analysis (TGA), Fourier transform infrared (FTIR) spectroscopy, and powder X-ray diffraction (XRD). Notably, the successful formation of the isobutanol ammonium salt was verified by the discernible differences in DSC curves between the parent drug and the salt form. Powder XRD analysis further provided evidence of a chemical reaction occurring between flurbiprofen and 2-amino-2-methylpropan-1-ol, resulting in the creation of a distinct salt entity. Solubility studies unequivocally demonstrated that the conversion of flurbiprofen into its salt form significantly increased its solubility. Thus, the conversion of flurbiprofen into an isobutanol ammonium salt offers a viable solution to address the inherent solubility challenge associated with this BCS Class II API. This transformation has the potential to substantially enhance the bio-availability of flurbiprofen and improve its therapeutic effectiveness.

Keywords: Flurbiprofen, pharmaceutical salts, bio-availability, absorption, aqueous solubility

ABBREVIATIONS

API- Active pharmaceutical ingredient, FLB: flurbiprofen, IBA:Isobutanol ammonium, BCS: Biopharmaceutical classification system, MHz: Mega Hertz.

INTRODUCTION

Preformulation is the process of applying biopharmaceutical principles to the physicochemical properties of a drug substance to build the best drug delivery system possible. The dissolution or absorption of drugs into the body is not always ideal because they are created as a weak acid or base. The therapeutic efficacy of a drug is ultimately determined by its bio-availability and solubility[1-3]. Drug compounds typically have numerous functional groups capable of hydrogen bonding because they are intended to connect with a receptor, enzyme, protein, etc. Some of these functional groups have the potential for salt formation[4-6]. This salt creation provides the pharmaceutical chemist and formulation scientist with the chance to alter the physicochemical and mechanical properties of the potential medicinal ingredient and to create dosage forms with excellent bio-availability, stability, manufacturability, and patient compliance[7-10].

One crucial factor in achieving the optimum medication concentration in the bloodstream, so that a pharmacological reaction can be seen, is solubility. More than 40% of new chemical entities created by the pharmaceutical industry are insoluble in water, necessitating salt production, because any medicine that is to be taken must be present as a solution at the absorption site. The choice of salt former depends significantly on the ionizable group's acidity or basicity, the counter ion's safety, and the pharmacological indications[11-13].

The pharmaceutical industry stands at the forefront of scientific innovation, striving to develop effective medications that can address a myriad of health conditions.

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Among the various challenges faced by drug developers, the solubility of active pharmaceutical ingredients (APIs) plays a pivotal role in determining a drug's bio-availability and therapeutic efficacy. Biopharmaceutical Classification System (BCS) classifies drugs into four categories based on their solubility and permeability characteristics, with BCS class II encompassing drugs that exhibit high permeability but poor solubility. Overcoming the solubility limitations of BCS Class II drugs represents a critical endeavor, as it can significantly impact drug formulation, dosage, and ultimately patient outcomes[14-17].

BCS Class II drugs include numerous vital therapeutic agents, ranging from anticancer compounds to cardiovascular medications, and anti-infective to central nervous system drugs. Despite their immense therapeutic potential, the limited solubility of these compounds often hinders their clinical translation. Low solubility leads to reduced bio-availability, necessitating higher doses, which can increase the risk of adverse effects and hinder patient compliance. Additionally, inadequate solubility poses manufacturing challenges, limiting formulation options, and driving up production costs. Consequently, it is essential to develop strategies to enhance the solubility of BCS Class II drugs, thus unlocking their full therapeutic potential. Flurbiprofen belongs to BCS class II drugs, hence the issue of it's low solubility must be resolved[18-21].

A salt called ibuprofen isobutanol ammonium was developed to relieve discomfort brought on by vaginal infections. The brand name of this product is Ginenorm®. Clinical data support the efficacy and tolerability of this salt, which was created particularly for gynecological use, in the management of vulvovaginal irritation. When used with other antimycotic and antibacterial drugs, studies have shown that ibuprofen isobutanol ammonium has a synergistic antimicrobial effect[22-25].

Flurbiprofen is a non-steroidal anti-inflammatory drug (NSAID), commonly used for its analgesic and anti-inflammatory properties. However, one of its significant drawbacks is its low solubility in aqueous media. This poor solubility poses a substantial challenge in drug formulation and limits its bio-availability when administered orally, leading to the need for high doses to achieve therapeutic effects. Addressing the solubility issue of flurbiprofen is crucial for optimizing its pharmacokinetics, reducing potential side effects associated with high doses, and enhancing its clinical utility in pain management and inflammation control. Chemically, flurbiprofen is (*RS*)-2-(2-fluorobiphenyl-4-yl)propanoic acid[26]. Various metal and metal amine salts of flurbiprofen like potassium, calcium, magnesium, choline, ethanolamine, ammonium, tromethamine, tertiary butyl amine and 2-amino-2-methyl-propan-1-ol were explored. The viscous liquid 2-amino-2-methyl-propan-1-ol(IBA) (Fig. 1) has a boiling point of 165 °C. Its pKa value is 9.7 and its molecular mass is 89.14 g mol^{-1} [27]. The parent drug and amine quickly interacted to produce a salt known as flurbiprofen isobutanol ammonium because the pKa difference between the amine and flurbiprofen is more than 2-3 units (FLB-IBA) (Fig. 1)[28-31].

In the pharmaceutical sector, it is crucial to analyze and characterize medicines as well as their salts. Even though the FLB-IBA salt has been described, we have presented a more detailed report on the synthesis and characterization of the flurbiprofen isobutanol ammonium salt in this study[32]. To comment on the solubility of the synthesized salt, we are focusing especially on solubility studies and dissolution assays, which will provide solid evidence for higher bio-availability of the salt in comparison to parent medication[33,34].

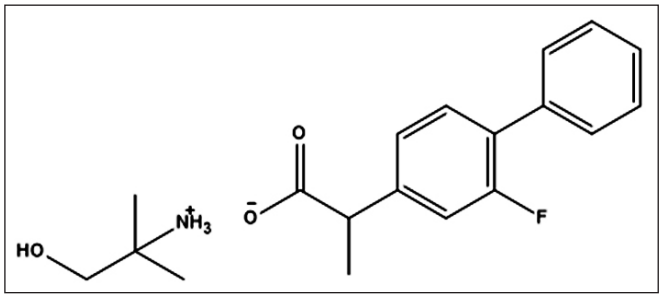

Fig. 1: Molecular structure of flurbiprofen isobutanol ammonium salt

MATERIALS AND METHODS

Materials

Except as otherwise noted, all chemicals and supplies were purchased from companies like Merck Ltd., Mumbai, India. and were as pure as was commercially practical. For synthesis, 99% pure 2-amino-2-methyl-propan-1-ol and 99% pure flurbiprofen were utilized. Toluene HPLC (99% purity) was used as the reaction's solvent during execution. Melting points were determined using the Veego instrument, specifically the VMP-DS model, in conjunction with a capillary melting point apparatus. The FTIR spectra of the API, salt former, and product were determined using the PerkinElmer spectrum 2 equipment. The scanning range for the samples was 4000-600 cm^{-1}. 5 mm NMR tubes were used to prepare samples for NMR research. For ^{1}H-NMR and ^{13}C-NMR, respective sample amounts of 10 mg and 20 mg were employed. The solvent utilized was DMSO. Tetramethyl silane (TMS) was

used as an internal standard and Agilent equipment was operated at 400 MHz to measure NMR. With the use of the MestReNova application's assessment version, the results were examined. The Shimadzu LABX instrument played a pivotal role in acquiring the PXRD patterns for both the API and its corresponding salt during the Powder X-ray diffraction investigation. Operational settings were set at 40kV and 30mA, with monochromatic Cuja radiation used to scan the samples across the range of 5 °C to 80 °C. For the DSC analysis, a PerkinElmer Pyris 6 instrument was used. 5 mg of the sample were heated between 35 and 600 °C at a rate of 20 k min^{-1} in a crumpled aluminum pan. For TGA analysis, a Shimadzu DTG-60H apparatus was employed. During the analysis, nitrogen was forced through aluminum pans at a rate of 30 mL min^{-1} [35-38].

Synthesis

10 mmoles (2.44 g) of the parent drug, flurbiprofen, were dissolved in 40 mL of toluene HPLC. 10 mmoles of 2-amino-2-methyl-propan-1-ol (0.954 mL) were added to the drug solution dropwise. The mixture was then stirred for 1h at room temperature using a Remi magnetic stirrer at 200 rpm. Buchner funnel was used to filter the precipitate that had developed. 1:1 combination of methanol and chloroform was used to recrystallize the products and dry at 50°C in an oven. To keep the salt generated dry and ready for further investigation, it was placed in a calcium chloride desiccator.

Solubility studies

To compare the influence of salt production on biopharmaceutical activity, solubility tests were conducted. Conducting solubility studies is of paramount importance in pharmaceutical research and development. These studies provide critical insights into the compound's ability to dissolve, which directly influences its bio-availability, formulation design, and overall efficacy, ultimately guiding the development of more effective and patient-friendly medications. We used the calibration curve method to find the solubility using a Shimadzu UV-2600 spectrophotometer. The aqueous salt solution was scanned to find the λ_{max} of salt. To generate the calibration curve, dilutions of 3, 6, 9, 12, 15, and 18 ppm were made and scanned at a predefined λ_{max} (246.5 nm). A saturated salt solution in 10 mL of water was prepared, and the mixture was then equilibrated for 24h at 37 °C on a Planetory shaker (Make-Neuation, Model number-iShak 3D-5) . After 24h, the solution was centrifuged on a Remi C30+ centrifuge for 10 minutes at 7000 rpm (rcf = 5000g). After appropriately diluting the filtrate, its absorbance at the maxima of salt was measured. The solubility of the salt was determined by calculating it by multiplying the measured absorbance by a dilution factor. Additionally, we established the solubility of the parent medication, flurbiprofen. Utilizing distilled water with a pH of 7, simulated gastric fluid (SGF) with a pH of 1.2, and simulated intestinal fluid (SIF) with a pH of 6.8, the solubility studies were conducted. To replicate real-world situations, SIF and SGF buffer solutions were also taken into consideration.

Dissolution assay

Dissolution assays are essential in pharmaceutical development, as they mimic how a drug will be released and become available for absorption in the body. These tests, play a pivotal role in ensuring consistent drug performance, batch-to-batch quality control, and formulation optimization. Accurate dissolution data informs regulatory decisions and helps to deliver safe, effective medications to patients. An *in vitro* dissolution study on the salt using simulated gastric fluid at pH 1.2 and simulated intestinal fluid at pH 6.8 were chosen. This analysis allows us to evaluate the solubility and release pattern of the salt under conditions mimicking the acidic environment of the stomach and the more neutral conditions of the intestines. Additionally, since the drug needs to be in a dissolved state for absorption and permeability to take place, we can also assess and comment on the salt's ability to permeate at these pH levels. To perform this assay, prepared Simulated Intestinal Fluid with a pH of 6.8 and Simulated Gastric Fluid with a pH of 1.2. To create 3 L of Simulated Gastric Fluid (SGF) with a pH of 1.2, 6 g of NaCl was dissolved in a minimum amount of distilled water, to which 21 mL of HCl was added, and the volume was then made up to 3 L with distilled water. Potassium dihydrogen phosphate (KH_2PO_4), 20.4 g, and 0.2 N NaOH were dissolved in distilled water to create 3 L of Simulated Intestinal Fluid (SIF), pH 6.8. The capacity was then filled to 3 L with distilled water. By adding 0. 1 N HCl, the buffer's final pH was brought down to 6.8.

A paddle-style USP dissolution type 2 device was utilized to carry out the *in vitro* dissolution assay. Buffers were added to the dissolution equipment vessels, and the water bath's temperature was changed to 37 °C. Once the required temperature was achieved, we affixed the paddles and promptly administered the calculated equivalent dose of the salt. To ensure accuracy, this assessment was conducted on two separate occasions. Withdrawal of 5 mL of the sample using a filtered syringe was followed by replenishing the buffer medium with an additional 5 mL of buffer solution. The samples were removed after 0, 5, 15, 30, 45, and 60 minutes for SGF and after 0, 30, 60, 90, 120, and 180 minutes for SIF. We determined the

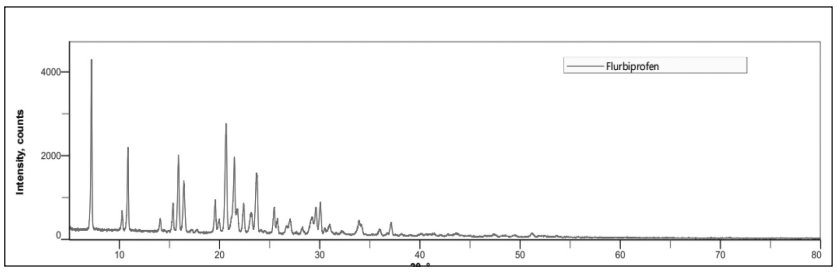

Fig. 2: PXRD curve of FLB

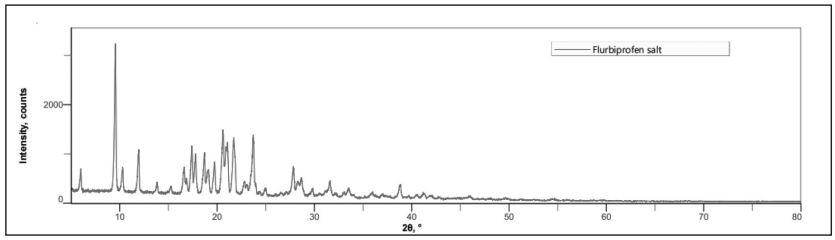

Fig. 3: PXRD curve of FLB-IBA salt

concentration of the samples by applying the standard curve equation, and their absorbance was assessed at 246.5 nm after proper dilution. To gain insights into the release pattern of the salt under different pH conditions, we constructed a graph plotting the percentage of drug release or dissolution against time.

RESULTS

Synthesized salts were characterized by analytical techniques such as Fourier transform infrared spectroscopy and Nuclear Magnetic Resonance spectroscopy. The interaction between the drug and salt former was then studied by Powder X-ray diffraction and thermal analytical methods such as DSC, DTG, and TG. The changes in the profiles of the drug and salt were then examined. UV spectroscopy was used for solubility studies. The melting point was determined using the Veego instrument, triplicate measurements were performed, and the data obtained was as follows; the melting point of flurbiprofen is 113 °C and that of flurbiprofen isobutanol ammonium salt is 160 °C. The yield for the salt was calculated to be 2.882 g (93%).

FTIR

FTIR spectra of flurbiprofen, 2-amino-2-methyl-propan-1-ol, and FLB-IBA salt were recorded, and spectra of API was compared to its salt for the purpose of characterization. FTIR spectrum of 2-amino-2-methyl-propan-1-ol shows bands at 1300-1000 cm^{-1}, 1472 cm^{-1}, 1596 cm^{-1}, 2962 cm^{-1}, 3600-3200 cm^{-1}. FTIR spectrum of FLB-IBA salt has bands at 2921 cm^{-1}, 3346 cm^{-1}, 1624 cm^{-1}, 1361 cm^{-1}.

NMR

NMR of FLB-IBA was determined to confirm salt formation. The data obtained from the spectra is as follows;

FLB-IBA salt: ^{1}H-NMR (400 MHz, DMSO-*d*6) δ 7.40 (d, J = 8.0 Hz, 4H), 7.02 (t, J = 8.7 Hz, 4H), 6.89 (t, J = 7.6 Hz, 3H), 6.71 (t, J = 7.4 Hz, 2H), 6.20 (d, J = 8.0 Hz, 2H), 3.36 (s, 6H), 3.04 (s, 6H), 2.46 (s, 2H), 2.09 (s, 1H), 0.89 (s, 15H).

^{13}C-NMR(101 MHz, DMSO-*d*6) δ 175.90, 175.87, 143.69, 143.53, 138.52, 138.41, 130.52, 129.44, 129.34,129.29, 128.82, 128.75, 126.09, 124.32, 124.28, 120.35, 120.26, 115.92, 71.70, 50.67, 44.75, 40.44, 40.23, 40.03, 39.82, 39.61, 39.40, 39.19, 27.09, 23.38.

PXRD

PXRD analyses were conducted to investigate the interactions between API and the salt former. The Figs. 2 & 3 depict the results from the PXRD experiment.

Thermal studies

It was possible to determine the DSC, DTG, and TG profiles of pure API and the equivalent salts, which provided details on endotherm, heat flow for breakdown, and stability. The discussion section examines the importance of the findings from thermal experiments.

Solubility studies

The flurbiprofen isobutanol ammonium salt calibration curve was plotted using an aqueous solution ranging from 3 to 18 ppm. Table I contains the data. Refer to Fig. 4 for the flurbiprofen isobutanol ammonium salt calibration curve.

Table I: Absorbance of flurbiprofen isobutanol ammonium measured at 246.5 nm

Concentration/ppm	Absorbance
3	0.2674
6	0.4688
9	0.6308
12	0.7797
15	0.9269
18	0.9982

Table II: Dissolution assay readings of the salt

A) Dissolution of flurbiprofen-IBA at simulated gastric pH of 1.2									
Time (mins)	**Absorbance**	**Dilution factor**	**Conc. (µg mL^{-1})**	**Conc. (µg mL^{-1}) *DF**	**Conc. (mg mL^{-1})**	**Conc. (mg $10mL^{-1}$)**	**Conc. (mg $900mL^{-1}$)**	**Amount of drug release**	**%Drug release**
0	0.156	1	1.9001	1.9001	0.00190	0.0190	1.71011	1.7101	0.441
5	0.16	1	1.9488	1.9488	0.00194	0.0194	1.75395	1.7539	0.452
15	0.203	1	2.4725	2.4725	0.00247	0.0247	2.2253	2.2253	0.574
30	0.245	1	2.9841	2.9841	0.00298	0.0298	2.6857	2.6857	0.693
45	0.366	1	4.4579	4.4579	0.00445	0.0445	4.0121	4.0121	1.035
60	0.636	1	7.7466	7.7466	0.00774	0.0774	6.9719	6.9719	1.799
B) Dissolution of flurbiprofen-IBA at simulated intestinal pH of 6.8									
Time (mins)	**Absorbance**	**Dilution factor**	**Conc (µg mL^{-1})**	**Conc (µg mL^{-1})*DF**	**Conc (mg mL^{-1})**	**Conc (mg $10mL^{-1}$)**	**Conc (mg $900mL^{-1}$)**	**Amount of drug release**	**%Drug release**
0	0.130	50	3.2581	162.907	0.162	1.629	146.616	146.616	37.849
30	0.160	50	4.0100	200.501	0.200	2.005	180.451	180.451	46.583
60	0.183	50	4.5864	229.323	0.229	2.293	206.390	206.390	53.280
90	0.206	50	5.1629	258.145	0.258	2.581	232.330	232.330	59.976
120	0.215	50	5.3884	269.423	0.269	2.694	242.481	242.481	62.596
180	0.228	50	5.7142	285.714	0.285	2.857	257.142	257.142	66.381

Using 1 mL of a saturated solution that had been equilibrated for 24 h, a total volume of 1000 mL was created. By taking 25 mL of this solution, it was diluted up to 100 mL. The dilution factor as a result is 4000. The three duplicate measurements yielded an average absorption value of 0.548.

To determine concentration of the solution after dilution , the linear equation was combined with the average absorbance value into the linear equation. By multiplying this concentration by the dilution factor, to the total amount of salt that could dissolve in 1 mL of water the solubility of flurbiprofen salt in water was found to be 31.09 mol mL^{-1}.

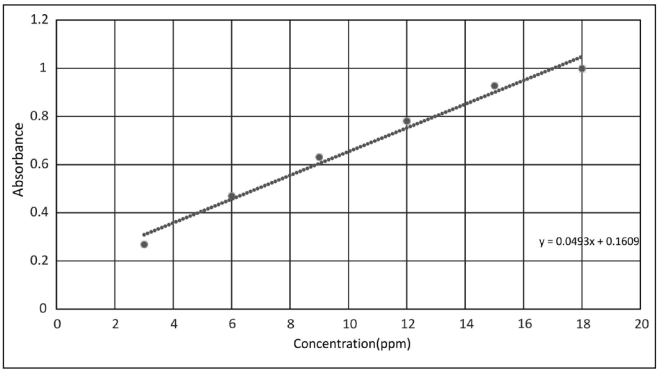

Fig. 4 : Calibration curve of flurbiprofen isobutanol ammonium salt

Dissolution Assay

The results of the experiment on dissolution are included in Table II.

CHN Analysis

1) The results from FLB-IBA salt CHN analysis are included in Table III.

Table III: CHN analysis report of FLB-IBA salt

Element name	Retention time (min)	Area (.1*uV*sec)	Element %
Nitrogen	0.775	218443	4.422
Carbon	1.092	7847195	68.687
Hydrogen	3.650	2610415	7.351

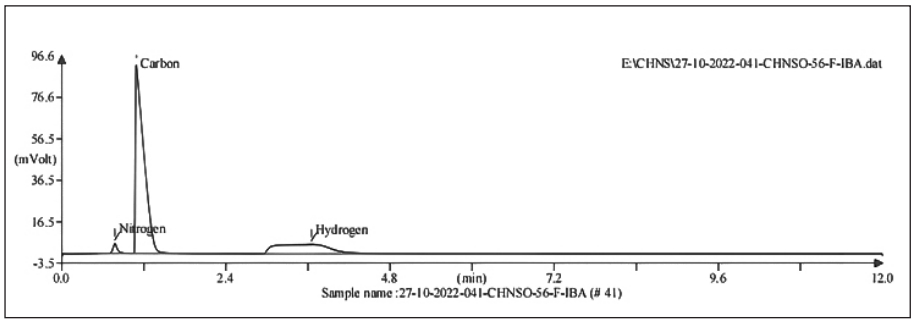

Fig. 5: CHN elemental analysis graph of FLB-IBA Salt

Refer to Fig. 5 for flurbiprofen isobutanol ammonium salt elemental analysis graph.

DISCUSSION

FTIR Analysis

The FTIR spectrum of 2-amino-2-methyl-propan-1-ol reveals significant features. A distinct signal at 1596 cm^{-1} indicates the presence of primary amines through N-H bending vibrations. Furthermore, a broad band spanning the 3600-3200 cm^{-1} region confirms the presence of the hydroxyl (OH) group. This band coincides with an aliphatic C-H stretch observed at 2962 cm^{-1} and the N-H stretching of the primary amine. Additionally, within

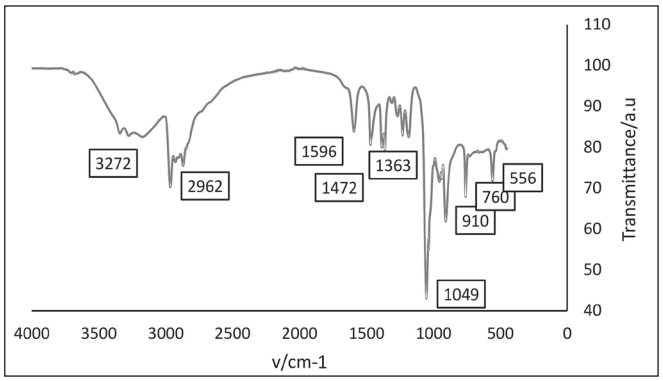

Fig. 6: IR spectra of 2-amino-2-methyl-propan-1-ol

the 1300-1000 cm^{-1} range, peaks signify the stretching vibrations associated with C-O and C-N bonds. Notably, alkane stretching vibrations have been detected at 1472 cm^{-1} (Fig. 6).

FTIR spectroscopy was used to examine the spectra of the flurbiprofen isobutanol ammonium salt and its precursors (flurbiprofen and 2-amino-2-methyl-propan-1-ol). The salts were found to lack the flurbiprofen molecule's distinctive CO stretching of the carboxylic acid group at position 1695 cm^{-1}. At 1624 cm^{-1} and 1361 cm^{-1}, bands resembling carboxylic acid salts took its place. Around 2921 cm^{-1}, there was an extra band that was caused by the NH_3^+ stretching of solid ammonium salt, which was overlapped by C-H alkene stretching. The free OH group stretching of salt former was observed at 3346 cm^{-1} (Fig. 7).

NMR

A peak corresponding to the amine salt is observed as a singlet in the flurbiprofen isobutanol ammonium NMR spectra at 2.46 ppm, which is otherwise noticeable at about 1.55 ppm in reference to AMP NMR spectra, clearly indicating the salt formation. According to the analysis, the carboxylic acid proton that was previously seen in the flurbiprofen spectra is no longer present in the NMR spectra of the FLB-IBA salt. The free OH of AMP is present at 0.89 ppm. The NMR spectra of flurbiprofen and the FLB-IBA salt are shown in Fig. 8 through Fig. 11.

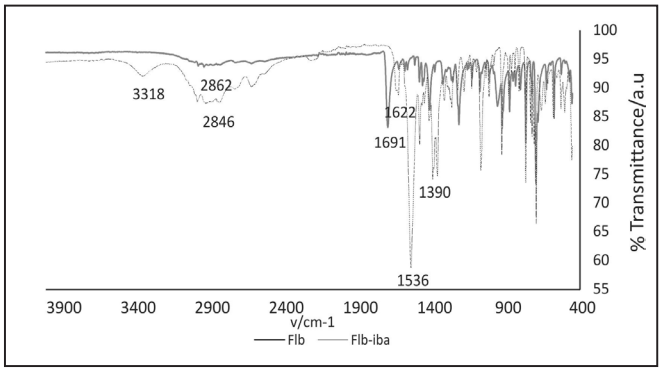

Fig. 7: FTIR spectra of flurbiprofen and FLB-IBA salt

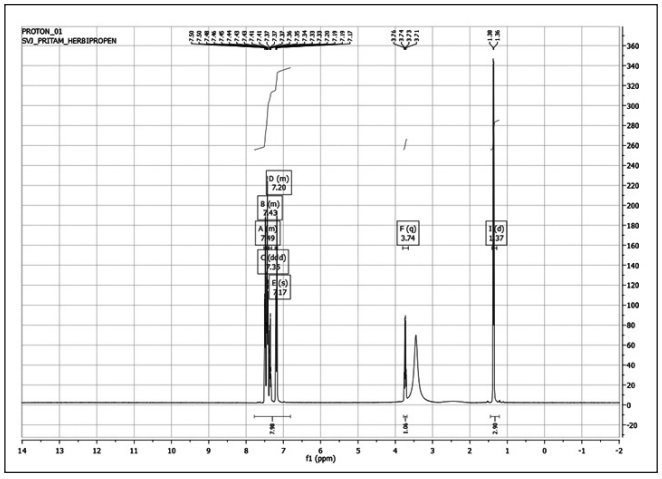

Fig. 8: 1H NMR of flurbiprofen

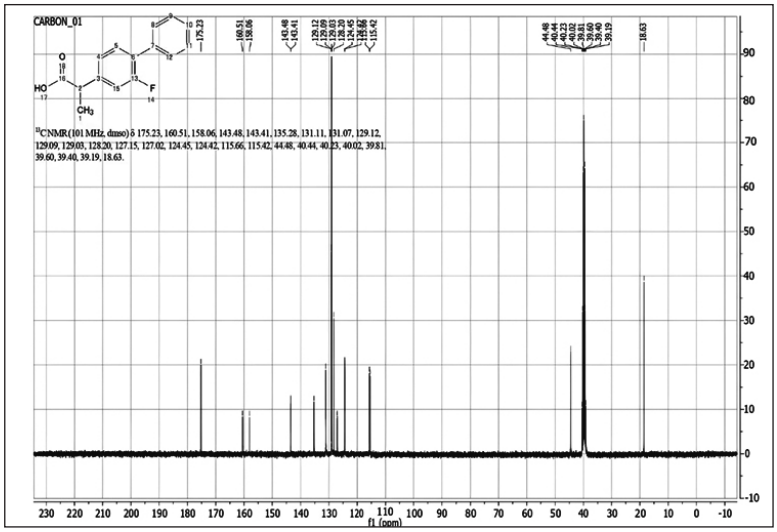

Fig. 9: 13C NMR of flurbiprofen

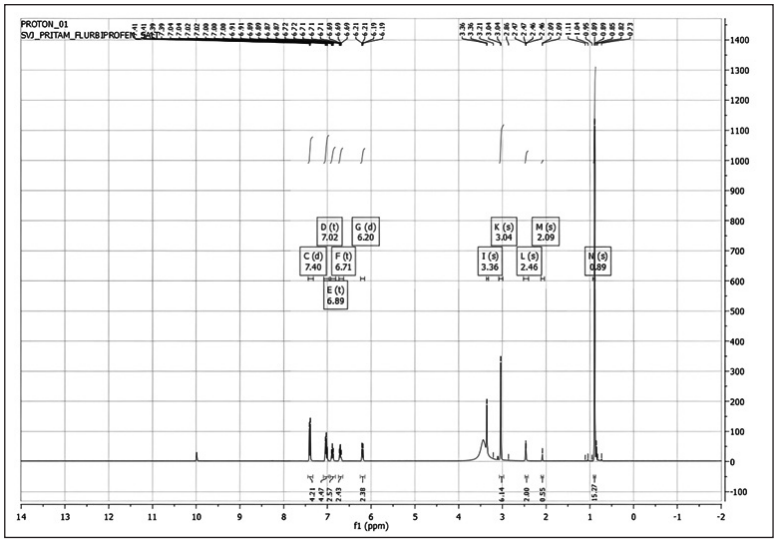

Fig. 10: 1H NMR of flurbiprofen isobutanol ammonium salt

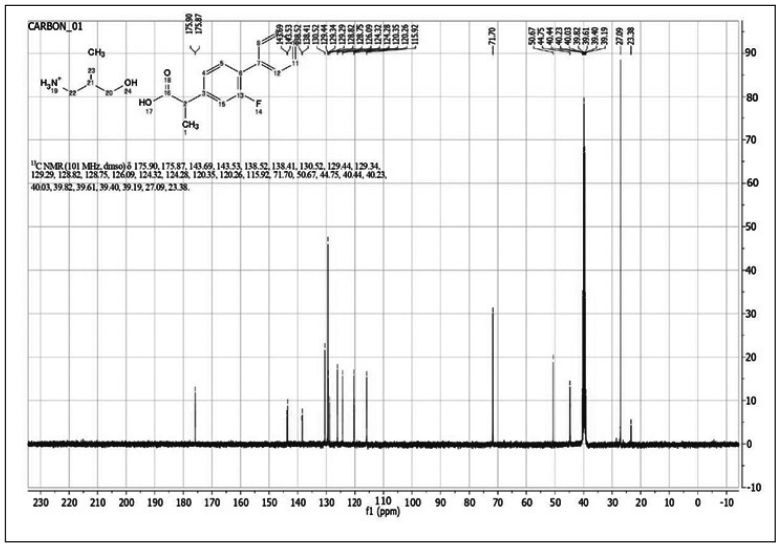

Fig. 11: 13C NMR of flurbiprofen isobutanol ammonium salt

Powder X-ray diffraction analysis

An alternative method used to validate the synthesis of the salt involved performing powder X-ray diffraction (PXRD). In Fig. 3, the PXRD graphs for the FLB-IBA salt reveal distinctive peaks unique to the salt, suggesting its distinct crystalline pattern. Furthermore, the presence of sharp peaks provides further evidence of the salt's crystalline nature, as well as its differentiation from the parent drug.

Thermal analysis

Using DSC and TGA, the thermal profiles of the flurbiprofen isobutanol ammonium salt were assessed. Fig. 12 displays the comparative thermal profile i.e. DSC, DTG, and TG heat flow curves for flurbiprofen and its isobutanol ammonium salts.

Flurbiprofen's DSC curve reveals the presence of an endotherm, with onset and peak temperatures of 113.15 °C and 118.21 °C, respectively. Further at around 400 °C, a decarboxylation peak can be seen.

The starting and sharp peak temperatures of the endothermic flurbiprofen isobutanol ammonium salt curve are 142.68°C and 158.57°C, respectively, while the second blunt peak represents the breakdown temperature. Sharp peaks demonstrate the crystallinity of flurbiprofen and flurbiprofen isobutanol ammonium salt. After investigation, it was found that the pure FLB and its salt differential thermogravimetric (DTG) profiles were distinct from one another, as illustrated in Fig. 7. Peak FLB and FLB-IBA mass change temperatures were 324°C and 326°C, respectively. Thus, the DTG profiles of the drug and its salt vary from one another.

Following analysis, it was discovered that the thermogravimetric (TG) properties of pure flurbiprofen and its salt were dissimilar. The graphs show a single breakdown mark for both the original medicine and its salt. The graph shows that the salt appears to be slightly less stable than flurbiprofen, with a breakdown temperature of T onset TG = 184.07°C as opposed to T onset TG of 244.13°C for flurbiprofen.

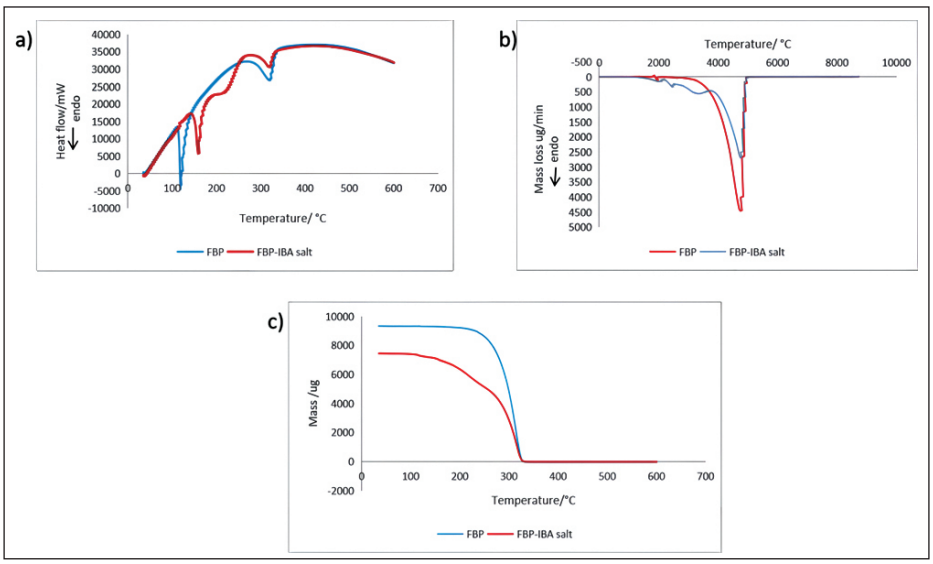

Fig. 12: Comparative thermal profiles a) DSC b) DTG c) TG of flurbiprofen and FLB-IBA Salt

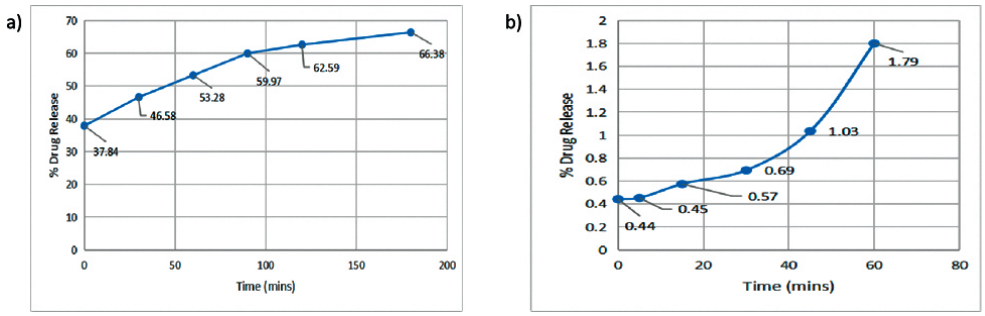

Fig. 13 Drug release profile curves of a)FLB-IBA at Simulated intestinal fluid (pH 6.8) and b)FLB-IBA at Simulated gastric fluid (pH 1.2)

Solubility studies

The solubility of FLB-IBA salt in water was found to be 31.09 mol mL^{-1}. Thus, there is a significant improvement in solubility as compared to pure flurbiprofen solubility which is reported as 0.000029 mol mL^{-1} and the drug bank (Pub-Chem) declared it to be insoluble. The results clearly demonstrated that the conversion of the API into its salt form significantly improved solubility, suggesting a promising strategy to enhance its bio-availability and overall therapeutic effectiveness. This underscores the crucial role of salt formation in optimizing biopharmaceutical properties[26].

Dissolution assay

Fig. 13 depicts the curve of % drug release versus time. It can be concluded from the data that dissolution of salt increases with an increase in pH, this can be confirmed by SIF(pH 6.8) data, where solubility is found to be much higher (60-70%). Drug release at SGF pH was found to be around 2-4%, indicating that salt absorption will not occur in the stomach. The release profile indicates that % drug release of FLB-IBA in gastric pH is 1.79 % and in intestinal pH is 66.38 %.

CONCLUSION

Using pure flurbiprofen (API) and 2-amino-2-methyl-propan-1-ol (salt former) as precursors, we successfully synthesized flurbiprofen isobutanol ammonium salt in this study. Techniques such as FTIR spectroscopy and powder XRD were used to justify salt formation. Flurbiprofen isobutanol ammonium salt's DSC heat flow curve had a melting endotherm with an onset and peak of 142.68 °C and 158.57 °C. The second endotherm indicates decomposition temperature; thus, salt was found to be more stable than parent drugs. Solubility analysis studies indicate improvement in solubility on salt formation as compared to pure flurbiprofen.

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