

Original Research Article

Enhancement of the dissolution profile of diclofenac sodium using ionic liquid-based formulations

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Abstract

Purpose: To investigate the dissolution profile of ionic liquid forms of diclofenac sodium.

Methods: Three ionic liquids, namely 1-butyl-3-methylimidazolium chloride, cholinium chloride, and benzalkonium chloride, were converted into corresponding diclofenac-ionic liquid formulations by reacting each ionic liquid with diclofenac sodium at a 1.1:1 molar ratio. The prepared diclofenac-ionic liquids were solidified by adsorption onto microcrystalline cellulose (Avicel PH-102) and characterized using Fourier-transform infrared spectroscopy, powder X-ray diffraction, and differential scanning calorimetry to prove ionic interactions as well as partial amorphization of the diclofenac.

Results: Percentage yield of the prepared ionic formulations was > 94 %. There was significant improvement in solubility, with the imidazolium diclofenac ionic liquid exhibiting a 5.3-fold and 4-fold increase in solubility in distilled water and phosphate buffer (pH 6.8), respectively ($p < 0.05$). In addition, the imidazolium diclofenac-ionic liquid showed an excellent dissolution profile.

Conclusion: These results highlight the potential applicability of imidazolium diclofenac ionic liquid as an efficient dissolution rate enhancer for diclofenac. This study justifies applying ionic liquids as recovery-enhancing carriers in drug delivery systems, especially for poorly soluble drugs.

Keywords: Diclofenac sodium, Ionic Liquids, Solubility Enhancement, Drug Dissolution

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INTRODUCTION

Diclofenac sodium (DC Na) is an analgesic, antipyretic, and anti-inflammatory nonsteroidal anti-inflammatory drug (NSAID) belonging to phenylacetic acid class. Unlike many conventional NSAIDs, DC Na has a more significant effect on cyclooxygenase (COX)-2 enzyme than COX-1. Also, DC Na has significant dose-dependent gastrointestinal, cardiovascular, and renal side effects, similar to other NSAIDs. The original purpose of developing delayed- and extended-release versions of DC Na was to enhance the safety profile and offer patients a convenient once-daily administration in chronic

pain [1]. Diclofenac falls in class II of the Biopharmaceutical Classification System (BCS), characterized by low aqueous solubility and high intestinal permeability [2]. The rate and extent of absorption through the gastrointestinal membranes are primarily determined by these characteristics, which also have significant impact on the bioavailability [1]. It is sparingly soluble in water, partially insoluble in chloroform, soluble in ethanol (96 percent), and freely soluble in methanol [3]. Several formulation approaches have been explored to improve the solubility of poorly water-soluble drugs, including size reduction, use of surfactants, salt formation, pH adjustment, complexation, prodrug, nanosization,

liposome preparation, and solid dispersion formation. Although each of these techniques has some advantages, they may be marred by several drawbacks, such as low stability in the long term, complexity in fabrication, and difficulty in scaling up [4]. In this regard, ionic liquids (ILs) are considered a new class of solvents, exhibiting promising pharmaceutical applications. Ionic liquids (ILs) are a class of organic salts that are in liquid phase at temperatures lower than 100°C, and they possess a range of distinctive physicochemical properties such as low volatility, thermal resistance, and extreme solvation capacity [5,6].

The diversity of ILs comes from the fact that they are designed with cations and anions chosen properly in such a way that they interact with the drug molecules in a well-defined manner and improve their solubility in aqueous or aqueous organic systems. It has been reported that ILs are effective in increasing the solubility and dissolution rate of poorly soluble drugs, e.g., ibuprofen and naproxen [7,8]. The present study investigated the use of some selected biocompatible ILs for improving the solubility and dissolution rate of Diclofenac sodium. Based on the physicochemical properties of the loaded drug, ILs were chosen according to their pharmaceutical acceptability (environmental risk assessment) and their ability to interact with the drug molecule by solvation and disruption of intermolecular H-bonding. The prepared DC Na-ILs were characterized by Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC), and X-ray Diffraction (XRD) analysis. Solubility studies using different IL-based formulations and their comparison with solubility in conventional solvent systems were done. In vitro dissolution studies were also conducted to assess the enhancement of drug release from solidified DC Na-ILs onto microcrystalline cellulose (Avicel PH-102).

EXPERIMENTAL

Preparation of diclofenac sodium - ionic liquids (DC Na-ILs)

Three ionic liquid formulations of DC Na were synthesized using solvent evaporation method [9]. Initially, DC Na was allowed to react with 1-Butyl-3-methylimidazolium chloride (BMIMCl; Bide Pharmatech Ltd. (Shanghai, China)), Cholinium chloride (ChCl), and Benzalkonium chloride (BkCl; Heowns Biochem Technologies Co., Ltd. (Tianjin, China)) to synthesize three DC Na-ionic liquids (DC Na-ILs) in a 1.1:1 (drug: ionic liquid). An accurately weighed amount of DC Na was dissolved in 200 mL of methanol

(Gailand Chemical Company (GCC), UK). Thereafter, different weights of ILs were dissolved in 50 mL of methanol, and the ionic liquid solution was added slowly to the DC Na-containing solution. The mixture was refluxed for approximately 12 h at 70 °C. The reaction mixtures were then stirred for an additional 12 h at room temperature to ensure complete ion exchange. The resulting solutions were vacuum filtered using a sintered glass funnel and subsequently evaporated under reduced pressure to remove the solvents. The DC Na-ILs were filtered and dried under reduced pressure with a moderate volume of acetone washing. This washing process was repeated at least three times until precipitation of sodium chloride (NaCl) no longer occurred. The products obtained were placed in a vacuum oven at 40 °C for 24 h to remove residual solvent [9].

Formulation of powder containing DC Na-ILs

Solidification technique was adopted to convert the DC Na-ILs into solid powder form with microcrystalline cellulose (Avicel PH-102) as the adsorbent carrier. For powdering, 1 g each of the DC Na-ILs was added to a clean mortar. Then, Avicel PH-102 was slowly introduced in different weights of 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, and 4.5 g, while stirring for homogenized adsorption and dispersion. The blended product was triturated properly to obtain a dry, uniform, and free-flowing powder, and the formula with the least amount of Avicel used was selected for further investigation. The end solid formulation was preserved in well-closed containers for further characterization [10].

Characterization of DC Na-ILs

Percentage yield

The yield of the synthesized DC Na-ILs was calculated practically to determine the effectiveness of each formula. It was computed by dividing the theoretical mass of DC Na-ILs by the practical mass of the prepared DC Na-ILs (Eq 1) [11].

$$\text{Yield (\%)} = \frac{\text{Practical weight}}{\text{Theoretical weight}} \times 100 \dots\dots\dots (1)$$

Evaluation of the formulated powder flowability

Angle of repose

Angle of repose was calculated using Eq 2.

$$\tan \theta = h/r \dots\dots\dots (2)$$

Where θ is the angle of repose obtained by calculating the $\tan^{-1}$, h is the distance from the lower tip of the funnel to a surface, and r is the radius of the resulting cone [12].

Bulk density

The powder (20 g) was transferred into a graduated cylinder and the initial volume was recorded. The bulk density was calculated using Eq 3 [12].

Bulk density = weight of powder/bulk volume (3)

Tapped density

The powder (20 g) was transferred into a graduated cylinder and the volume occupied by the bed was obtained. The cylinder was tapped on a padded surface until no further change in powder volume was observed and the final volume was recorded (Eq 4) [13].

Tapped density = weight of powder/tapped volume (4)

Hausner's ratio

It is the ratio between tapped and bulk density (Eq 5).

Hausner's ratio (HR) = tapped density/bulk density (5)

Determination of saturated solubility

The DC Na and the prepared DC Na-ILs were prepared in a tightly closed conical flask containing specific volume of distilled water, phosphate buffer solutions at pH 6.8, and methanol. The sample was shaken in a water bath maintained at 37 °C for 48 h, centrifuged at 1,000 revolutions per minute (rpm) for 30 min until equilibrium existed. The supernatant solutions were filtered using syringe filters (pore size of 0.22 μm) and analyzed spectrophotometrically. Three determinations were taken to estimate the saturation solubility value [14]. In accordance with solubility results, the optimum formula was then selected and subjected to further specification analysis.

In vitro dissolution studies

The powdered formulation of the DC Na-ILs obtained after solidification was filled into hard gelatin capsules using the manual filling method. Each capsule contained approximately 25 mg of DC-Na (Table 1).

Table 1: Lactose quantities to prepare 500 mg capsules for dissolution study

Formula	DC Na-ILs (mg) equivalent to 25 mg DC Na	Lactose (mg)
DC Na (control)	25	475
BMIM-DC Na	140	360
Cho-DC Na	60.5	439.5
BK-DC Na	238	262

In vitro dissolution of diclofenac sodium and the prepared formulas was determined using a USP type II (paddle method) by dispersing a quantity equivalent to 25 mg of diclofenac sodium in phosphate buffer (pH 6.8, 900 mL). The temperature was set using a thermostatic water bath at 37.0 ± 0.5 °C with a rotation speed of 50 rpm. At regular intervals, 5 mL were taken out and replaced with fresh dissolution medium to maintain sink conditions. They were then filtered using filter paper, and the drug content was spectrophotometrically determined at 276.5 nm. This test was performed on the formula for every sample, and carried out in triplicate [15]. In addition, a difference factor (f_1) and a similarity factor (f_2) were used in a basic model-independent method for analyzing the dissolution profiles [16].

Formulation of powder containing DC Na-IL

After converting the DC Na-ILs formulations into solid dosage form (powder) by adsorption onto microcrystalline cellulose (Avicel PH-102), the resulting powders were evaluated for their physical characteristics. Among the ratios used of Avicel, the BMIM-DC Na needed 0.75 g of Avicel to be converted to powder. In comparison, 2.5 and 3.5 g of Avicel were needed to convert CH-DC and BK-DC, respectively. With these ratios, the formulas exhibited an acceptable physical property (Table 2).

Table 2: Avicel quantities needed to convert the DC Na-ILs into solid powder

Avicel PH-102 (g)	Cho-DC	BMIM-DC	BK-DC
0.25	Sticky	Sticky	Sticky
0.5	Sticky	Sticky	Sticky
0.75	Powder	Sticky	Sticky
1	Powder	Sticky	Sticky
1.5	Powder	Sticky	Sticky
2	Powder	Sticky	Sticky
2.5	Powder	Powder	Sticky
3	Powder	Powder	Sticky
3.5	Powder	Powder	Powder
4	Powder	Powder	Powder
4.5	Powder	Powder	Powder

Characterization of the selected formula (DC-IL)

Following the characterization of the prepared DC Na-ILs, the formula that possessed acceptable physical properties was selected for further characterization.

Fourier transform infrared spectroscopy (FTIR)

The FTIR spectroscopy of DC Na, ILs, and DC Na-ILs was studied to identify the characteristics of functional groups of DC Na and detect any possible chemical interactions in its formulations.

The studied samples were pressed with KBr in disk form (13 mm in diameter) and analyzed from 400 to 4000 cm^{-1} at a resolution of 4 cm^{-1} with a scan speed of 2 mm/sec [17].

Differential scanning calorimetry (DSC)

Each sample (5 mg) was placed in a non-hermetically sealed aluminum pan and heated at a rate of 10°C/min over temperatures of 25 to 300 °C. The thermogram was obtained under inert conditions with continuous nitrogen purging (50 mL/min) [18].

Powder X-ray diffraction (PXRD)

PXRD is a technique used to determine the crystalline properties of powdered material by analyzing the diffraction pattern of X-rays passing through it. Samples of DC Na, ILs, and the selected formula were assessed by PXRD analysis using a PAN analytical X'Pert diffractometer with Cu K α radiation ($\lambda = 1.5406$ Å) as a source of x-ray and scanning from 10° to 80° 2 θ at a step size of 0.05° and 1 s/step, under fixed slit conditions at 25 °C [19].

Statistical analysis

Data analysis was carried out using Microsoft Excel software (Microsoft Inc.). Data were analyzed for mean and standard deviations (SD) of triplicate determination. Analysis of variance (ANOVA) was computed, and $p < 0.05$ was considered significant.

RESULTS

Percentage yield

The prepared formulation exhibited good percent yields (> 94 %), indicating the efficiency of the ILs synthesis (Table 3). The slight differences may be related to the chemical structure and

physical properties of the cation used (i.e., viscosity and hydrophilicity).

Table 3: Percentage yield of the prepared DA Na-IL formula

Formula	Yield (%)
BMIM-DC Na	94.43
Cho-DC Na	98.5
BK-DC Na	96.5

Physical characteristics of diclofenac sodium - ionic liquids (DC Na-ILs)

Three different DC Na-ILs were obtained, each one differing from the other in several characteristics (color, consistency, rheology, and physicochemical properties; Figure 1).

Powdered formulations obtained after solidification of DC Na-ILs

The formula that took the least amount of Avicel to be converted to powder was chosen for further processing. The optimized powder appeared as fine, free-flowing, and homogenous, indicating uniform distribution of the drug and Avicel (Figure 2).

Powder flow

The flowability study indicated that Cho-DCNa possessed better flow properties than others. The angle of repose, Carr's index, and Hausner's ratio were the lowest in Cho-DC Na formulation (26.57 °, 15.3 %, and 1.18, respectively), indicating lower interparticle cohesion and excellent flow. The results indicate that the choice of ionic liquid cation significantly influences powder flow properties, as reflected by angle of repose, Carr's index and Hausner ratio values (Table 4).

Determination of saturated solubility

Distilled water

Results showed that the solubility of DC-Na was enhanced in ionic liquids (ILs) with various organic cations. BMIM-DC Na showed an increase in solubility to a greater extent (≈ 5.3 -fold increase), while Cho-DC Na exhibited moderate solubility (≈ 2 -folds increase) compared to DC Na as a result of the strong hydrogen bonding between cations (imidazolium or cholinium) and the diclofenac carboxylate, and higher water affinity, which stabilizes the ionic structure in the solutions. Furthermore, BK-DC Na showed a slight increase in solubility compared to DC-Na because it is a more lipophilic IL (Figure 3).

Table 4: Flow properties of the DC Na-ILs

Parameter	BMIM-DC Na	Cho-DC Na	BK-DC Na
Angle of repose	44.45	26.57	35.29
Bulk density (g/mL)	0.249	0.424	0.379
Tapped density (g/mL)	0.384	0.5	0.522
Carr's index	35.2	15.3	27.4
Hausner's ratio	1.54	1.18	1.38
Flow characters	Poor flowable	Good flowability	Poor flowable

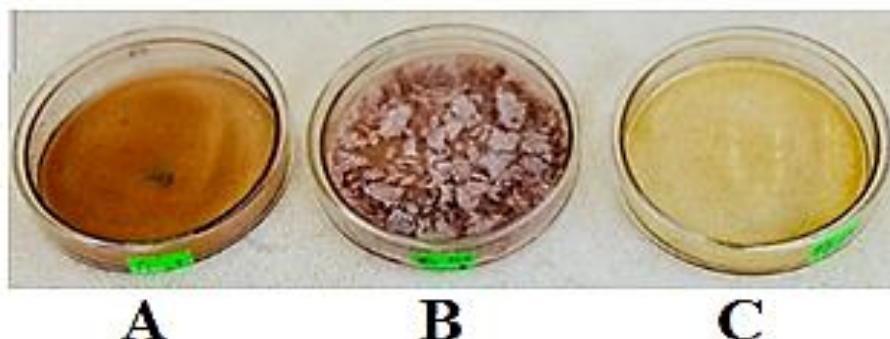


Figure 1: The DC Na-ILs with different organic cations. BMIM-DC (A) formed a homogeneous brownish ionic liquid, Cho-DC (B) yielded a pinkish semisolid indicative of a eutectic-like system, and BK-DC (C) formed a clear yellowish solution with good transparency and fluidity



Figure 2: Photographic representation of the powdered formulations obtained after solidification of DC Na-ILs. BMIM-DC (a), Cho-DC (b), and BK-DC (c)

Methanol

In methanol, solubility differences were minimal because both pure diclofenac and the ionic liquid forms exhibit high affinity for polar organic solvents, reducing the observable contrast between formulations. At the same time, the DC-Na was freely soluble in methanol, but the BMIM-DC Na showed more solubility than the pure drug (Figure 4). The saturation solubility of DC-Na in phosphate buffer (pH 6.8) showed very low solubility due to pKa (around 4), which indicates the pH at which it is 50 % ionized. At pH values below the pKa, the drug existed predominantly in its non-ionized, acidic form. Also, the

presence of ionic liquid improved the solubility of DC-Na in phosphate buffer (6.8; Figure 5).

In vitro dissolution studies

In *in vitro* dissolution studies, the cumulative amount of DC-Na release over time was compared with three different DC Na-ILs-based formulations. The release of BK-DC Na was less than that of the control (DC Na), while CH-DC Na showed comparable release to that of pure drug. The highest cumulative release appeared with BMIM-DC Na, where the release reached 90 % within the first 50 min, indicating a higher rate of solubilization.

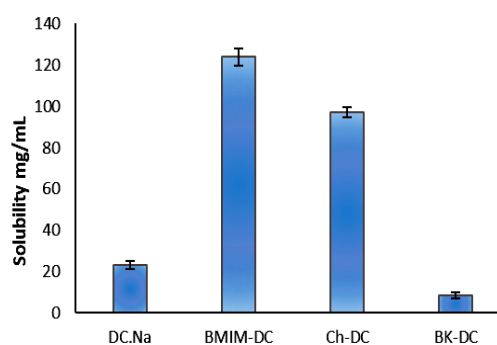


Figure 3: Saturation solubility of DC Sodium and prepared DC Na-ILs in distilled water (mean + SD, n = 3)

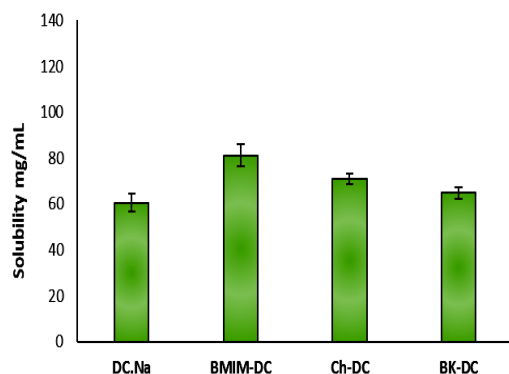


Figure 4: Saturation solubility of DC sodium and prepared DC Na-ILs in methanol (mean + SD, n = 3)

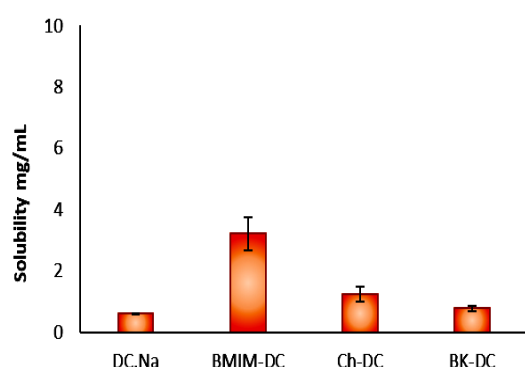


Figure 5: Saturation solubility of DC sodium and prepared DC-ILs in phosphate buffer (pH 6.8; mean + SD, n = 3). The BMIM-DC Na was selected as the optimum formula and subjected to further specification analysis

The imidazolium-based system of the tested formulations achieved the best enhancement with difference factor (f1) and a similarity factor (f2) equal to more than 50 and less than 50, respectively (Figure 6).

Evaluation of the selected formula (BMIM-DC)

Fourier transform infrared (FTIR)

The FTIR spectroscopy was used to study the molecular interactions between diclofenac sodium and ionic liquid components in the optimized formula. FTIR spectra of DC Na showed sufficient absorption bands at 3385.07 and 3257.77 cm^{-1} (N–H stretching), 1573.91 cm^{-1} of asymmetric stretching of the carbonyl group (CO), which confirmed matching with the standard FTIR of pure drug (Figure 7) while the FTIR of BMIM Cl- showed peaks at 2922.16 and 2852.72 cm^{-1} , which correspond to the aliphatic asymmetric and symmetric (C–H) stretching vibrations attributed to methyl groups (Figure 7).

Differential scanning calorimetry (DSC)

The DSC thermogram of diclofenac sodium (Figure 8 A) showed two transitions at temperatures of 41.91 °C, 77.45 °C, and 279.98 °C, is related to thermal decomposition or degradation. The thermal properties of BMIMCl (Figure 8 B) exhibited a single, sharp melting point at 72.36 °C, suggesting a high purity of the ionic liquid. The thermogram of the selected formula (Figure 8 C) showed a wide endothermic transition (112.83–130.54 °C).

Powder X-ray diffraction (XRD)

The DC-Na formulation exhibited a sharp diffractogram between 10° and 40°, indicating a crystalline structure with long-range order of molecules (Figure 9 A). Pure 1-Butyl-3-methylimidazolium Chloride showed a prominent peak between approximately 20–30° 2 θ , characteristic of semi-crystalline or amorphous materials, indicating short-range order without distinct crystalline peaks (Figure 9 B).

The XRD pattern of the selected BMIM-DC formulation displayed broad, diffuse halos with no prominent sharp peaks, confirming amorphization and successful disruption of the crystalline lattice of diclofenac sodium (Figure 9 C).

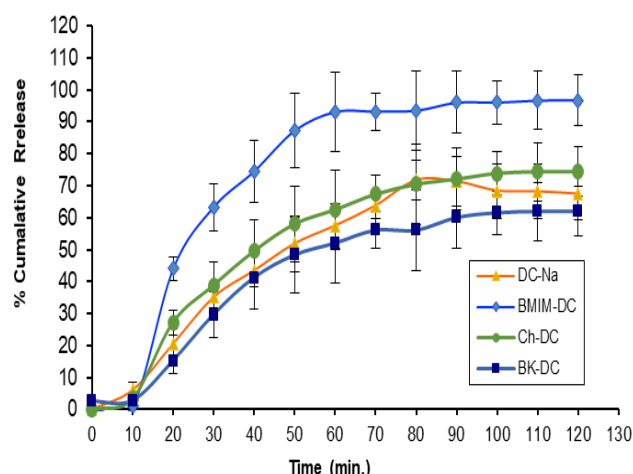


Figure 6: *In vitro* dissolution profile of diclofenac sodium with different ionic liquid carriers (mean + SD, n = 3)

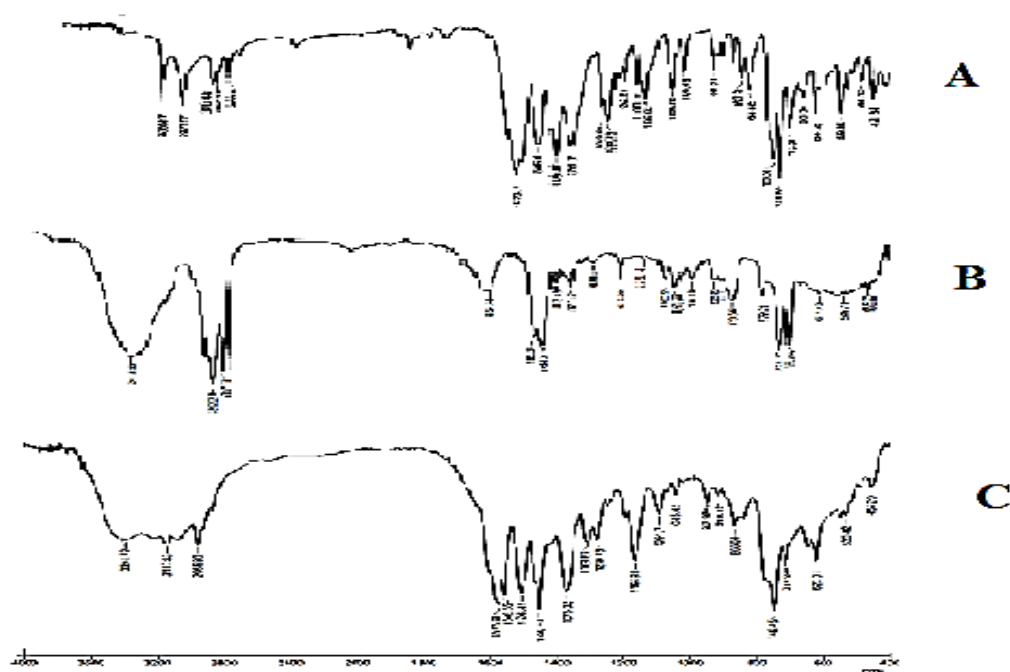


Figure 7: FTIR spectrum of pure DC sodium (A), BMIMCl (B), and BMIM-DC (C)

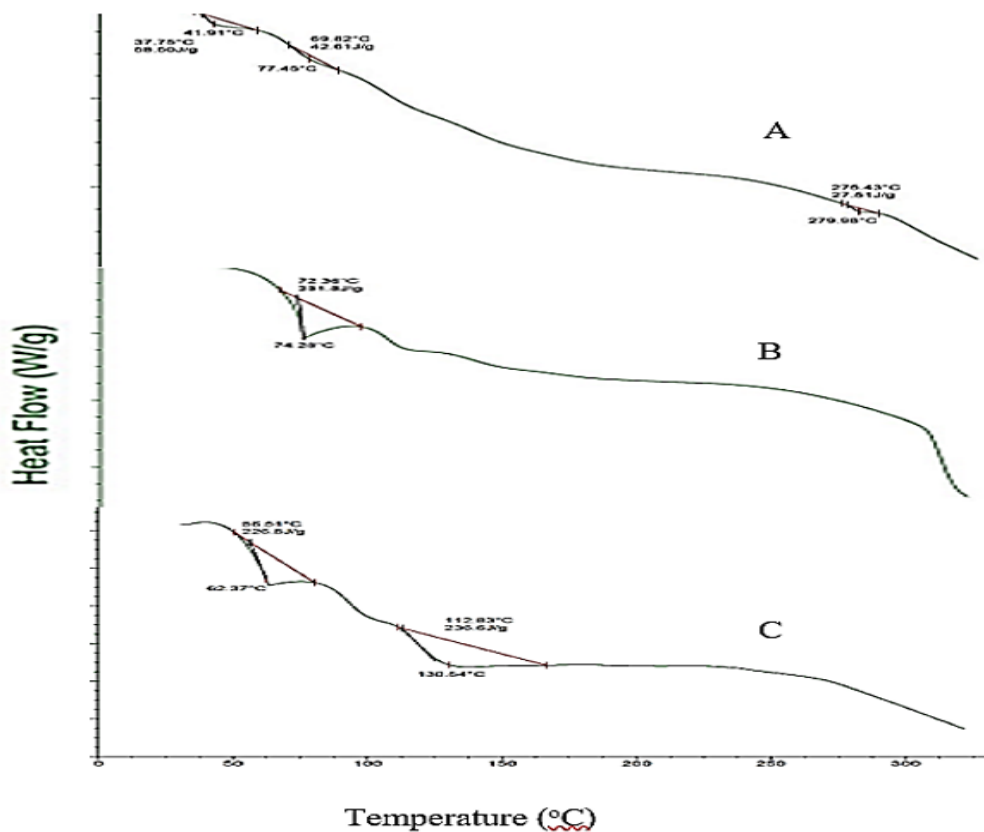


Figure 8: DSC thermogram of (A) pure DC sodium, (B) 1-butyl-3-methylimidazolium chloride, (C) Optimized formula BMIM-DC

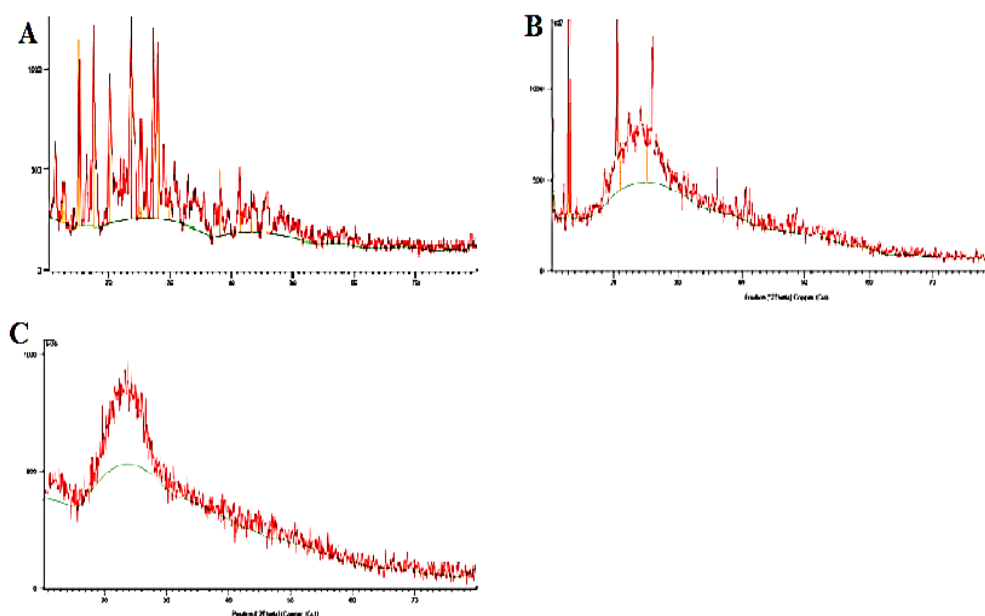


Figure 9: XRD diffractograms of pure DC Na (A), 1-butyl-3-methylimidazolium chloride (B), optimized formula BMIM-DC (C)

DISCUSSION

Generally, ionic liquids (ILs) are salts containing poorly coordinated anions and cations at room temperature (RT) or below 100 °C. They are also called ionic fluids, ionic melts, liquid electrolytes, fused salts, liquid salts, ionic glasses, designer solvents, green solvents, and, in recent times, referred to as solvents of the future [20]. Ionic liquids (ILs) are composed of ions with distinctive properties such as high thermal stability, high solvating power, and low vapor pressure [21]. These features of ILs are very useful in pharmaceutical drug discovery, development of new solvents for chemical synthesis, development of new drug delivery systems (such as nanoparticles and micellar systems for targeted delivery, and creating solid dispersions, which can improve the bioavailability and solubility of the drugs [22]. This study, therefore, investigated some selected biocompatible ILs for improving the solubility and dissolution rate of Diclofenac sodium. The yield obtained was similar to previous studies that synthesized a collection of cholinium-based ionic liquids, with yields between 95 and 100 %, demonstrating the effectiveness of the ionic liquid preparation technique [2]. The flowability study indicated that Cho-DCNa possessed better flow properties compared to others. The angle of repose, Carr's index, and Hausner's ratio were the lowest in Cho-DC Na formulation (26.57 °, 15.3 %, and 1.18, respectively), indicating lower interparticle cohesion and excellent flow [19]. As opposed to the BMIM-DC Na, which revealed poor flowability

as it showed a high angle of repose (44.45°), Carr's index (35.2 %), and Hausner's ratio (1.54), indicating a high degree of particle cohesiveness or irregular particle shape. The BK-DC Na also had poor flowability. One of the most essential practical parameters in drug release studies is the medium that can maintain sink conditions. Sink condition is the volume of media, which should be 3-10 times greater than that needed to produce a saturated solution of the drug substance [23].

The saturation solubility study in distilled water (DW) showed that the solubility of DC-Na was dramatically enhanced in ionic liquids (ILs) with various organic cations. However, BMIM-DC Na showed an increase in solubility up to 5.3-fold, while Cho-DC Na exhibited medium extent of solubility ($\approx$ 2-fold increase) compared to DC Na. This is as a result of the strong hydrogen bonding between cations (imidazolium or cholinium) and the diclofenac carboxylate, and higher water affinity, which can stabilize the ionic structure in the solutions. The BK-DC Na showed a slight increase in solubility compared to DC-Na because it is a more lipophilic IL that weakly interacts with water [24]. While in methanol, there was no significant change in solubility between the drug and its formulas. This outcome is due to methanol being a strong polar solvent that dissolves a wide range of organic compounds. At the same time, the DC-Na is freely soluble in methanol, but still the BMIM-DC Na showed more solubility than that of the pure drug. The enhancement of DC Na and its ILs solubilities

comes from the strong hydrogen bonding between methanol and the ILs components, π - π stacking between the imidazolium ring and diclofenac, hence reducing the lattice energy of the drug, thereby allowing its solvation [25]. The ionic liquid offers a versatile approach to enhancing the solubility of weak

acids like diclofenac, thus modifying their interactions with the solvent and disrupting their tendency to aggregate, which can further affect the ionization state of the acid or its interactions with the buffer, leading to improved dissolution in phosphate buffers [2]. The imidazolium-based system of the tested formulations achieved the best enhancement with difference factor (f1) and a similarity factor (f2) equal to more than 50 and less than 50, respectively [18]. In addition, it reached the maximum peak release at an early point. This marked increase in dissolution is attributed to the remarkable solubilization effect of imidazolium-ionic liquid [26].

FTIR spectra of DC Na showed sufficient absorption bands at 3385.07 cm^{-1} and 3257.77 cm^{-1} (N-H stretching), 1573.91 cm^{-1} of asymmetric stretching of the carbonyl group (CO), which confirmed matching with the standard FTIR of pure drug while the FTIR of BMIM Cl showed peaks at 2922.16 and 2852.72 cm^{-1} , which correspond to the aliphatic asymmetric and symmetric (C-H) stretching vibrations attributed to methyl groups. A prominent peak in the range of 3415.93 cm^{-1} was attributed to the production of quaternary amine salts with chlorine. The FTIR of the selected formula, BMIM-DC Na, exhibited remarkable shifts and alterations relative to the individual spectra of pure DC-Na and BMIMCl. The wide O-H/N-H band at 3394 cm^{-1} , the altered carboxylate stretching bands (1570 – 1624 cm^{-1}), and the emergence of C-N/C-Cl interactions in the 1000 – 1250 cm^{-1} range substantiate the synthesis of a novel ionic liquid salt via proton transfer and ionic interaction between the diclofenac anion and the 1-butyl-3-methylimidazolium cation. The spectrum alterations signify chemical interaction and the creation of a new chemical entity having different physicochemical properties compared with the starting materials [27].

The DSC thermogram of diclofenac sodium showed two transitions at temperatures of 41.91°C and 77.45°C , which proceed without mass variation on the thermogravimetric curve. They are associated with endothermic effects and are likely the consequence of structural rearrangements (polymorphic transformations) [27]. Another peak at 279.98°C is related to

thermal decomposition or degradation [3]. The thermal properties of BMIMCl exhibited a single, sharp melting point at 72.36°C with a high enthalpy, reflecting the high purity of ionic liquid. The DSC thermogram of the selected formula showed a wide endothermic transition (112.83 – 130.54°C). These transitions indicate the successful formation of a new compound: (BMIM-DC Na) that has specific thermal behavior compared to the parent compound (DC-Na). The high melting/decomposition temperature of pure DC-Na (279.98°C) was absent or decreased, due to the rupturing of its crystalline lattice by the ionic liquid. The DC-Na formulation exhibited sharp diffractogram between 10° and 40° , indicating crystalline structure with long-range order of molecules. The slow reduction of intensity after 40° is expected in normal scattering behavior. Pure 1-Butyl-3-methylimidazolium Chloride showed a prominent peak between approximately 20 – 30° 2θ , characteristic of semi-crystalline or amorphous materials, indicating short-range order without distinct crystalline peaks. The pattern exhibits a deficiency of numerous strong, high-intensity peaks, indicating low crystallinity or a disordered structure. The progressive reduction in intensity beyond 30° corroborates the amorphous/semi-crystalline characteristics. The XRD pattern of the selected formula reveals the absence of a sharp and well-defined peak, indicating a predominantly amorphous structure and the lack of crystal characteristics compared with the pure drug, meaning successful disruption of the crystalline structure of diclofenac sodium by creation of BMIM-DC.

CONCLUSION

The present study successfully demonstrates the capability of ionic liquid-based formulations to improve the solubility and dissolution characteristics of Diclofenac sodium. Characterization by FTIR, XRD, and DSC confirms the formation of a new ionic complex with modified molecular interactions, low crystallinity, different thermal behaviors, and improved physicochemical properties. The improved dissolution profile noted for BMIM-DC indicates the possibility of imidazolium-based ionic liquids as effective carriers for poorly water-soluble pharmaceuticals. These findings offer compelling reasons for the continued exploration of ionic liquid-based techniques as novel instruments in pharmaceutical formulation to address solubility-restricted bioavailability.

DECLARATIONS

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None.

Ethical approval

None provided.

Use of Artificial intelligence/Large language models

We also declare that we did not use Generative artificial intelligence (AI) and AI-assisted technologies in writing the manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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