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Synthesis and Physiochemical Studies of Ibuprofen Ionic Liquid

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Abstract: *Block chain technology has gained significant attention in recent years due to its potential to revolutionize various industries. This research paper explores the applications, challenges, and future directions of Block chain technology. It provides an overview of Block chain fundamentals, examines its real-world applications across different sectors, discusses the challenges and limitations associated with Block chain implementation, and explores future directions with a specific example*

Keywords: Block chain

I. INTRODUCTION

Ionic liquids (ILs) are normally defined as compounds completely composed of ions with melting point below 100 °C. ILs as innovative fluids has received wide attention only during the past two decades. The number of SCI papers published on ILs has exponentially increased from a few in 1996 to >5000 in 2016. These substances are variously called liquid electrolytes, ionic melts, ionic fluids, fused salts, liquid salts, or ionic glasses. [1,14,13]

According to their properties and characteristics, ILs are categorized into three generations.

- The first generations of ionic liquids were mainly on their intrinsic physical and chemical properties *viz.* Solubility, chemical/thermal stability, density and conductivity.
- The second generation included the tune of various physical and chemical properties which led to the formation of "Task specific ionic liquids".
- The third and most recent generation involves active pharmaceutical ingredients that are used to produce ionic liquids with biological activity. [2,14,13]

The ionic bond is usually stronger than the Van der Waals forces between the molecules of ordinary liquids. Because of these strong interactions, salts tend to have high lattice energies, manifested in high melting points. Some salts, especially those with organic cations, have low lattice energies and thus are liquid at or below room temperature. Ionic Liquids are often moderate to poor conductors of electricity, non-ionizing. They exhibit low vapor pressure. Many have low combustibility and are thermally stable. The solubility properties of ILs are diverse. [3,14,13]

The discovery date of the "first" ionic liquid is disputed, along with the identity of its discoverer. Ethanolammonium nitrate (M.P. 52–55 °C) was reported in 1888 by S. Gabriel and J. Weiner. One of the earliest room temperature ionic liquids was ethylammonium nitrate (M.P. 12 °C), reported in 1914 by Paul Walden. Different solubility techniques have been used to enhance its solubility but mostly used technique is solid dispersion. [4]

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) that is used to relieve pain, fever, and inflammation. This includes painful menstrual periods, migraines, and rheumatoid arthritis. It can be used by mouth or intravenously. Adverse effects include nausea, indigestion, diarrhea, constipation, gastrointestinal ulceration/bleeding, headache, dizziness, rash, salt and fluid retention, and high blood pressure, Cardiovascular risk. It typically begins working within an hour. Common side effects include heartburn and a rash. Compared to other NSAIDs, it may have other side effects such as gastrointestinal bleeding. It increases the risk of heart failure, kidney failure, and liver failure. At low doses, it does not appear to increase the risk of heart attack; however, at higher doses it may. Ibuprofen can also worsen asthma. While its safety in early pregnancy is unclear, it appears to be harmful in later pregnancy, so is not recommended. Along with several other NSAIDs, chronic ibuprofen use has been found correlated with risk of progression to hypertension in women and myocardial infarction (heart attack), particularly among those chronically using higher doses. [5,6,7,12]

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Like other NSAIDs, it works by inhibiting the production of prostaglandins by decreasing the activity of the enzyme cyclooxygenase (COX). Ibuprofen is a weaker anti-inflammatory agent than other NSAIDs. The main mechanism of action of ibuprofen is the non-selective, reversible inhibition of the cyclooxygenase enzymes COX-1 and COX-2 (coded for by *PTGS1* and *PTGS2*, respectively; In-vitro studies have indicated that, of the two enantiomers, *S*-ibuprofen is a more potent inhibitor of COX enzymes compared with *R*-ibuprofen. [8,12]

In an in-vitro human whole-blood assay, *S*-ibuprofen was seen to have comparable inhibitory activities toward COX-1 and COX-2 (IC50 2.1 and 1.6 µmol/l, respectively). In contrast, *R*-ibuprofen was ~ 15-fold less potent than *S*-ibuprofen as a COX-1 inhibitor (IC50 34.9 µmol/l) and did not inhibit COX-2 at concentrations of up to 250 µmol/l. [9,12]

COX-1 and COX-2 catalyze the first committed step in the synthesis of prostanoids – prostaglandin (PG) E2, PGD2, PGF2α, PGI2 (also known as prostacyclin), and thromboxane (Tx) A2 – from arachidonic acid. Prostanoids produce a diverse array of biologic effects through the activation of prostanoid receptors, and play important roles in a variety of homeostatic and pathologic processes. [10,12]

Ibuprofen is a large non-polar molecule which is insoluble in water in its molecular form. The molecular form of ibuprofen reacts as a carboxylic acid and will form a water-soluble salt upon its reaction with sodium carbonate solution. The sodium salt of ibuprofen is water-soluble due to the newly acquired ability to form stronger inter molecular forces (ion-dipole) with polar water molecules. Ibuprofen has a poor water solubility with less than 1 mg of ibuprofen dissolving in 1 ml water. It is more soluble in aqueous alcohol mixtures. Ibuprofen is an example of a poorly water-soluble drug from the Class II drugs of the BCS, with low solubility and high permeability. [11,12]

For the present study, Ibuprofen is used for the synthesis of API-based ILs because of its poor solubility. Ibuprofen is used as anionic. The objective of the present study is to synthesize Ibuprofen-IL by combination of cations and anions, improve its physicochemical properties and evaluate its biological activity.

II. REVIEW OF LITERATURE

Zhigang Lei' Biaohua Chen**et. Al. (2017)**[1] Discussed about Ionic liquid in details.

- **Ferraz R. et.al. (2011)**[2] Discussed about various generations of ILs
- **Welton** T.**et.al. (2018)** [3] Ionic Liquids: a brief history. Biophhysics Reviews.
- **Douglas R.et.al. (2001)** [4] Discussed low viscosity ionic liquids based on organic salts of the dicyanamide anion
- **Busson M. et.al. (1986)**[5]Update on Ibuprofen: Review Article. Journal of International Medical Research.
- **Kantor T. et.al.(1979)** [6] Ibuprofen. Annals of Internal Medicine.
- **NezvalováH. et.al. (2013)**[7] Effects of ibuprofen, diclofenac, naproxen, and piroxicam on the course of pregnancy and pregnancy outcome: a prospective cohort study.
- **Gierse J. K. et.al. (1999)** [8]Kinetic basis for selective inhibition of cyclo-oxygenases.
- **Neupert W. et.al. (1997)**[9] Effects of ibuprofen enantiomers and its coenzyme A thioester on human prostaglandin endoperoxide synthases.
- **Smyth E. M. et.al. (2008)** [10] Prostanoids in health and disease.
- **Álvarez, C. et. al. (2011)**[11]Investigation on the Possibility of Biowaivers for Ibuprofen.
- **Krasniqi. et. al. (2019)** [12]"The use of Ibuprofen and our knowledge about it" (2019). UBT International Conference.
- **Egorova K. S.et.al.(2017)** [13] Biological Activity of Ionic Liquids and Their Application in Pharmaceutics and Medicine.
- **Pedro S, et.al. (2020)**[14]The Role of Ionic Liquids in the Pharmaceutical Field: An Overview of Relevant Applications.

III. RATIONALE BEHIND SELECTION OF TOPIC

Crystalline forms of API are often preferred due to their improved physicochemical properties. However, most of the drugs lag behind due to polymorphic conversion, low solubility and low bioavailability for crystalline solids and the

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tendency of amorphous form to crystallize. Until date, various techniques have been developed; to improve these physicochemical parameters, ionic liquids is one of them.

Ionic liquids are prepared by judicious choice of cat-ions and anions with melting point below 100^0 C. API-based ionic liquids, the third generation of ionic liquids have been synthesized, in order to improve physicochemical properties like solubility, dissolution profile, Log P, etc. and the biological activity of API. In synthesis, API is either used as cat-ion or anion. However, the literature survey reveals that, API-ILs are designed in three types, the first type of ILs is via ionic bonding, where API is used as cat-ion or anion, the second type of ILs is via covalent linkage while similar or different API are combined in one IL in which API-IL with dual activities is produced in the third type of ILs.

IV. AIM AND OBJECTIVES

4.1 Aim

To synthesize Ibuprofen-ILs, improve its physicochemical properties and evaluate its biological activity.

4.2 Objectives

- To synthesize the ionic liquids of Ibuprofen by Solvent Evaporation Method.
- To characterize the ionic liquid by, IR Spectroscopy, Differential Scanning Calorimetry (DSC), X-ray diffractometry (XRD).
- Investigate physicochemical characteristics, Saturation Solubility, Release Rate Evaluation, Partition Co-efficient

V. PLAN OF WORK

The following experimental protocol was designed to allow a systemic approach to the study:

1. Literature survey.
2. Selection of drug.
3. Selection of method.
4. Procurement of drugs and chemicals.
5. Pre-formulation study
6. Optimization of batches
7. Synthesis of ionic liquids
8. Determination of Melting point
9. Characterization by
    a. DSC
    b. XRD
    c. IR spectroscopy
10. Saturation solubility determination
11. Partition coefficient
12. Dissolution study
13. Result and discussion.
14. Summary and Conclusion
15. Future Perspectives

VI. MATERIALS & EQUIPMENTS

Table 6.1: Drugs and chemical list

Sr. No	Name of Chemical	Sources
1	Ibuprofen	Research Lab Fine Chem Industries, Mumbai
2	Ethanol	Changshu Hongsheng Fine Chemical Co. Ltd
3	Tetra Methyl Ammonium Bromide	Loba Chemie Pvt Ltd, Mumbai

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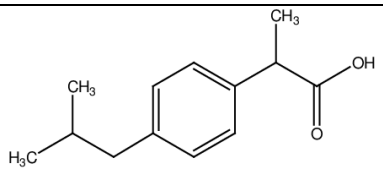
Table 6.2: Equipment's list

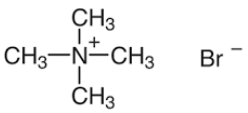
Sr. No.	Name of Instrument	Make & Model
1	Digital Balance	Wensar
2	UV Spectrophotometer	Shimadzu 1780
3	IR Spectrophotometer	Bruker-Alpha
4	Differential Scanning Calorimetry	SDT Q 600 V20.9 Build 20
5	Digital Melting Point Apparatus	Coslab

VII. EXPERIMENTAL WORK

Ibuprofen

Name	Ibuprofen
Category	NSAID
Chemical name	Iso-butyl phenyl propionicacid
Structure	 Ibuprofen
Synonym	Motrin, Brufen, Advil, etc
Molecular formula	C13H18O2
Molecular weight	206.28 g/mol
Solubility	Very soluble in alcohol
Melting point	75-77.5^0 C
Absorption	Rapidly and completely absorbed following oral administration
Bioavailability	102.7%
Protein binding	Ibuprofen dosage is more than 99% bound to plasma proteins and site II of purified albumin
Half life	1.8/ 2 hour
Metabolism	Ibuprofen is rapidly metabolized and biotransformed in the liver to the formation of major metabolites which are the hydroxylated and carboxylated derivatives
Drug interaction	Beta blockers, diuretics, warfarin
Adverse effect	Bloating, nausea, vomiting
Use dose	400 mg every 4-6 hours
Administration	Oral, Parenteral

Tetra Methyl Ammonium Bromide

Name	Tetra Methyl Ammonium Bromide
Structure	
Molecular formula	C8H20NBr
Molecular weight	154.05 g/mol
Description	White crystalline powder

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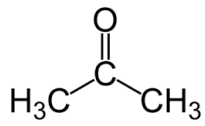
Solubility	Water
Melting point	M.P>> 300^0 C
Hydrogen bond acceptor	1
Hydrogen bond donor	0
Uses	Intermediate, Agriculture chemicals

Ethanol

Name	Ethyl alcohol (Ethanol)
Structure	
Molecular formula	CH3CH2OH
Molecular weight	46.08 g/mol
Description	Clear colorless liquid
Solubility	Water
Melting point	M.P. -114.1.C
Uses	Synthesis of Organic Solvent

7.1 Drug Authentication and Evaluation of Formulation

Ibuprofen was kindly provided by Research Lab Fine Chem Industries, Mumbai and was procured from Unique Laboratories, Kolhapur. The drugs were authenticated by melting point, UV spectra, IR spectra, DSC and XRPD.

Melting point:

The melting point of Ibuprofen was determined by Capillary method using Digital Melting Apparatus (Coslab) in which drug was placed into thin walled capillary tube having length 10-15 cm and 1 mm in diameter. This capillary was then placed in the beaker containing silicone oil. The heater and stirrer was kept on. The progress in temperature was monitored. The point at which drug started melting was noted and the experiment was carried out three times. The mean melting point was considered as melting point of drug.

UV Analysis:

The purity of Ibuprofen was determined by checking λ_{max} of drug by using Shimadzu UV 1780 Spectrophotometer.

Differential scanning calorimetry (DSC):

DSC analyzer (TA Instruments SDT Q600 USA) was used to perform the thermal analysis of pure Ibuprofen, ILs. A sample (5mg) was heated under a air atmosphere at a heating rate of 10^0C/min over the temperature range of 0-250^0 C

Fourier transformation-infrared spectroscopy (FTIR):

FTIR stands for "Fourier transform infrared" and it is the most common form of infrared spectroscopy which enables samples to be examined directly in the solid or liquid state without further preparation. FTIR (Bruker-ALPHA 100508) was used for the IR analysis of all samples. The samples were directly placed on the sample pan and analyzed from 600 to 4000 cm^{-1} spectral range with 24 scans.

X-ray powder diffractometry (XPRD): X-ray diffractometer (Bruker – D2 PHA-SER, Germany) with tube anode Cu was used to record XPRD patterns of all systems over the interval 10-$90^0/2\theta$. The operational data were as follows: Generator tension (voltage) 30 kV, Generator current 10 mA.

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Analytical method I:

Ibuprofen:

Preparation of standard solution of Ibuprofen in Ethanol system:

5mg of drug was accurately weighed and dissolved in 40 ml of Ethanol and 10 ml Distilled water, sonicated for few minutes and then volume was then adjusted upto 50 ml.

Scanning of Ibuprofen for λ_{max} in Ethanol system:

The absorption maximum of the standard solution was scanned between 200-400 nm regions on Shimadzu UV 1780 Spectrophotometer. The absorption maximum was found to be 261 nm.

Procedure: From the standard stock solution, aliquots of 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0 were withdrawn and transferred to the series of 10 ml volumetric flasks and final volume was made up to 10 ml with an Ethanol solution, Absorbance of this solution was measured against 261.20nm Ethanol as blank using Shimadzu UV 1780 Spectrophotometer.

Analytical Method II:

Optimization of batches Ibuprofen IL was prepared by using anions. Therefore, optimization of batches was done by determination of melting point which should be below 100^0C. The saturation solubility, dissolution rate, partition coefficient studies was also taken into consideration. The results revealed that IL of Ibuprofen and Tetra Methyl Ammonium Bromide with 1:1 ratio gave best results. These cation-anion combinations were further used to synthesize ILs.

Synthesis and characterization of optimized batch of Ionic Liquids(IL)

Synthesis:

Ibuprofen -IL was synthesized by adopting solvent evaporation method.Ratios of 1:1 of Ibuprofen and Tetra Methyl Ammonium Bromide were added to ethanol separately and dissolved. The clear solutions were obtained. These solutions were left for 7 days for solvent evaporation.

Analytical Method Development - I of ILs

Determination of λ_{max} of Ibuprofen-ILs

5 mg of Ibuprofen IL was accurately weighed and was dissolved in some quantity of Ethanol, volume was adjusted up to 50 ml. The standard solution was prepared with 100 µg/ml concentration. The absorption maximum of the standard solution was scanned between 200-400 nm regions on Shimadzu UV 1780 Spectrophotometer. The absorption maximum was found to be 265.60 nm in Ethanol system

Preparation of Calibration curve

5 mg of IL 1:1 was accurately weighed and dissolved in 5 ml of Water, then volume was then adjusted up to 50 ml with distilled water. The standard stock solution obtained was of 100µg/ml. From the standard stock solution, aliquot of 0.1, 0.2, 0.3, 0.4, 0.5, 0.6. were withdrawn and transferred to the series of 10 ml volumetric flasks and volume was made up to 10 ml. Absorbance of this solution was measured as water as blank at 265.60 nm using Shimadzu UV 1780 Spectrophotometer

Analytical method development –II of ILs

Determination of partition coefficient (log P)

The partition coefficient was determined by adding 10 ml each of n-octanol and water in glass tubes. It was allowed to stand overnight for 24 h at room temperature. Accurately weighed 25 mg of drug and IL was added to the tubes and stirred on magnetic stirrer for 24 h at 25oC. These mixtures were then transferred to the separating funnel and allowed to stand about 4 h for equilibration. Separation of aqueous and organic phases occurred. The concentrations of

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Ibuprofen and its IL were analyzed spectrophotometrically (Shimadzu 1780, Japan) at 223 nm respective. The formula used to calculate partition coefficient was,

Partition coefficient (logP) = log (Octanol/C water)

Where,C- is the concentration of drug in octanol and/or water phase.

VIII. RESULTS AND DISCUSSION

8.1 Drug Authentication

8.1.1 Melting Point:

The melting point of Ibuprofen was found to be in the range of 76 ^{o}C .The standard melting point of Ibuprofen 75-76 ^{o}C respectively.

8.1.2 UV Analysis:

The λ_{max} of Ibuprofen in ethanol was found to be 223 nm. The standard stock solution of fluconazole was scanned in the range of 200-400 nm to determine λ_{max}. The UV spectrum obtained is given below:

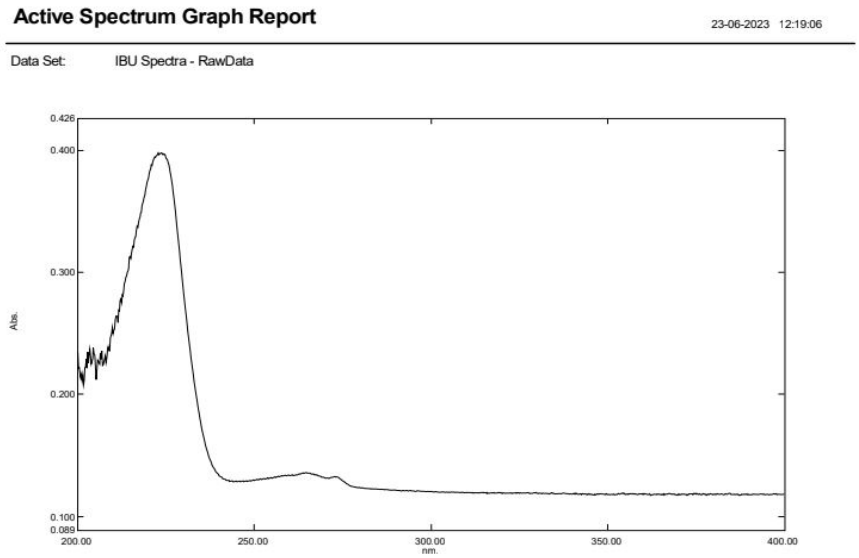

Figure 8.1 : UV spectra of Ibuprofen in ethanol

8.1.3 IR Analysis

IR spectra of Ibuprofen showed Principle absorption peak at 1457.19 (CH_2 , aliphatic), 1376.06 (CH3,aliphatic), 2954.61 (O-H stretch), 1717.40 (C=0, stretch), 1577.87, 1507.21 (C=C, aromatic stretch).

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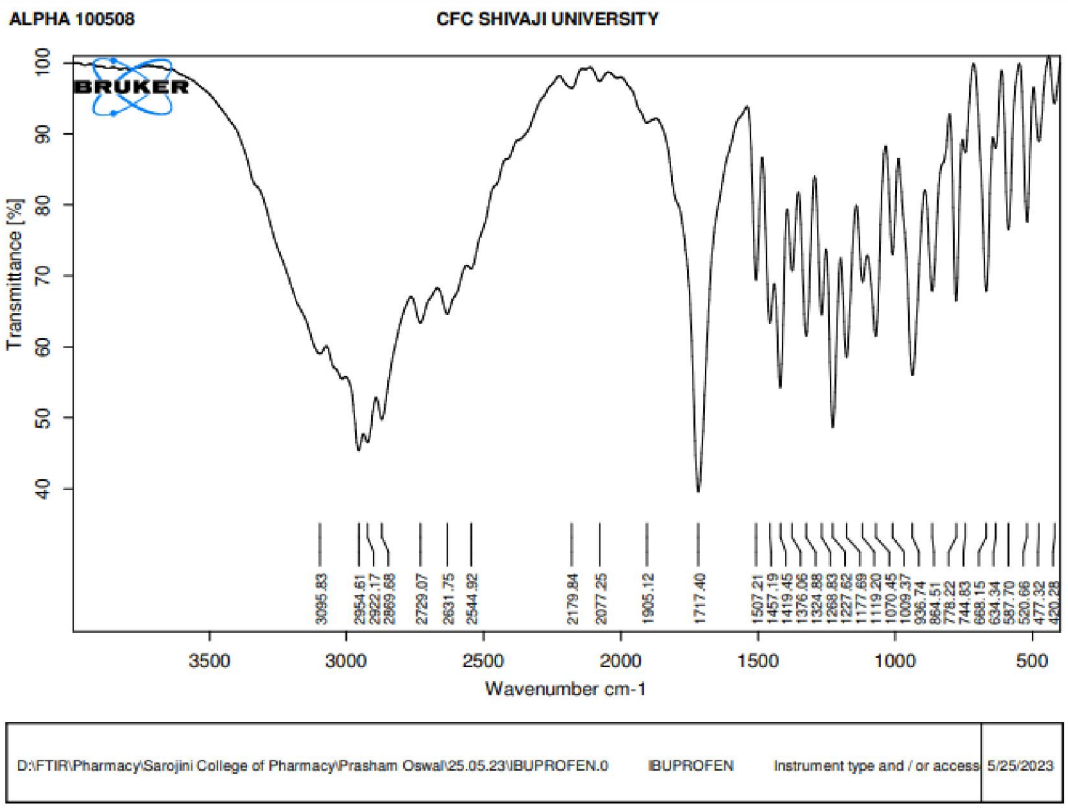

Figure 8.2: IR Spectra of Ibuprofen

8.1.4 DSC:

The DSC thermogram of Ibuprofen showed initially no peaks indicating amorphous nature but as the temperature was increased it showed exothermic peak at 80.53^{0}C indicating the crystalline nature while tetra methyl ammonium bromide showed peak sharp melting endothermic peak at389.77^{o}C.

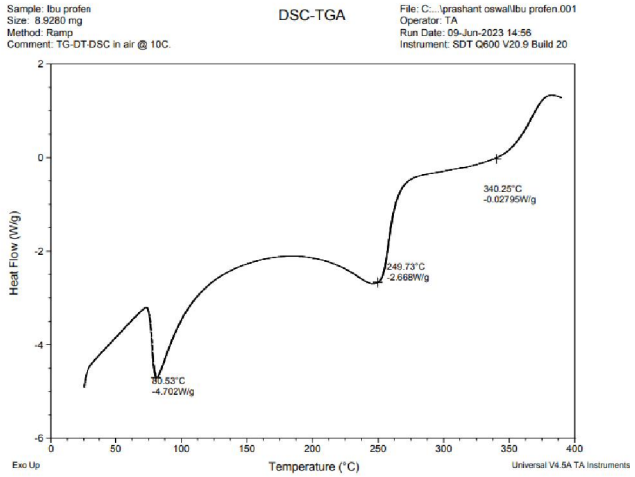

Figure 8.3: DSC Thermogram pure Ibuprofen

8.1.5 XRPD:

The sharp diffraction pattern with high intensity peaks in between 2θ angles of 10^o to 90^o as shown in XRPD of Ibuprofen in figure. This implies crystalline nature of both.

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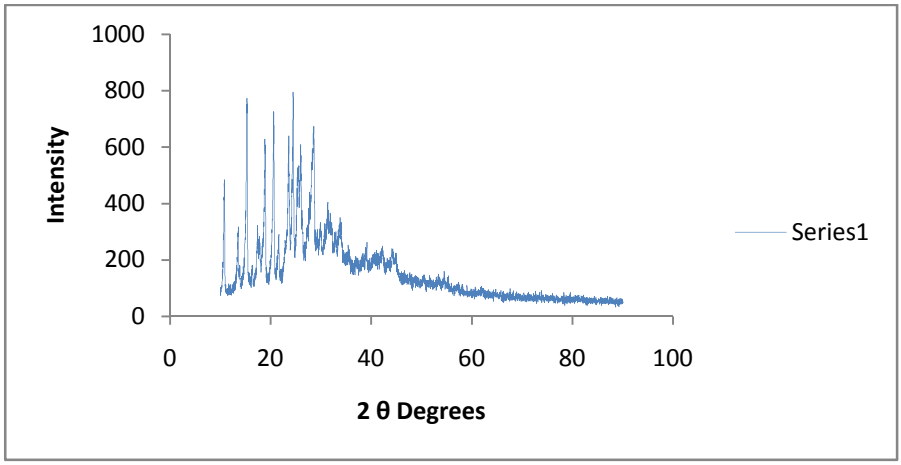

Figure 8.4: X-ray powder diffractogram of Ibuprofen

8.2 Analytical Method Development

8.2.1 Analytical method I:

Table 8.1: Calibration curve observations of Ibuprofen in ethanol: water (5:5)

Sr. No	Concentration (µg/ml)	Absorbance (A)
1	0.5	0.142
2	1	0.256
3	1.5	0.398
4	2	0.525
5	2.5	0.635
6	3	0.785
7	3.5	0.894
8	4	1.035

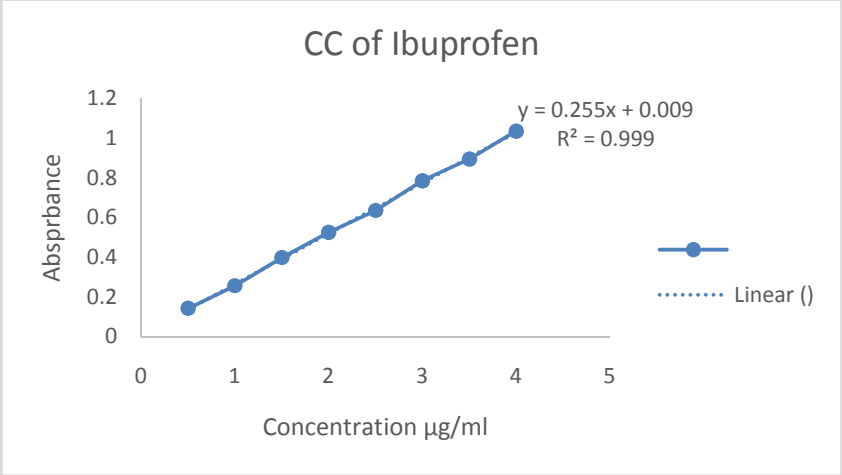

Figure 8.5: Calibration curve of Ibuprofen in ethanol-water(4:1)

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8.2.2 Analytical method II:

Table 8.2: Calibration curve observations of Ibuprofen in 0.1 N HCl

Sr. No	Concentration (µg/ml)	Absorbance (A)
1	2	0.122
2	4	0.201
3	6	0.300
4	8	0.391
5	10	0.473
6	12	0.565
7	14	0.683
8	16	0.757
9	18	0.851
10	20	0.927
11	22	1.048

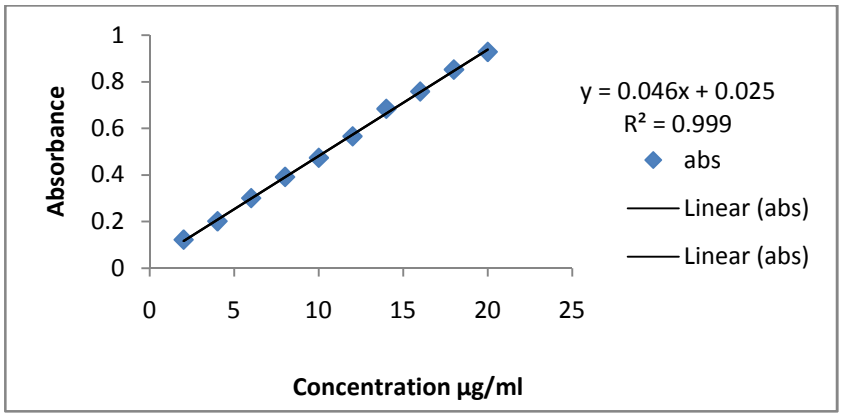

Figure 8.6: Calibration curve of Ibuprofen in 0.1 N HCl

8.3 Synthesis of Ibuprofen-ionic liquid:

The whitecrystalline solid compound pure Ibuprofen with tetra methyl ammonium bromide, after dissolving in acetone and complete solvent evaporation for 5 days appeared to be white compound with melting point below 100°C.As not all the ionic liquids are liquid at room temperature, ibuprofen–ionic liquid appeared to be in solid form at room temperature. The formation of Ibuprofen-IL was confirmed by its melting point. Photograph of Ibuprofen ionic liquid is given below,

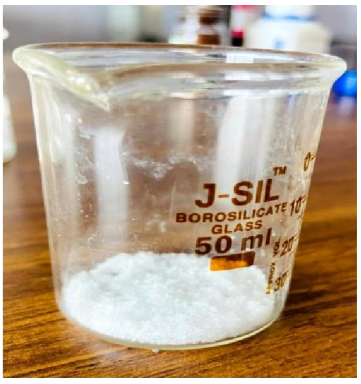

Figure 8.7: Photograph of Ibuprofen ionic liquid.

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8.4 Melting point determination

The melting point of Ibuprofen 76 °C and its ionic liquid 89 °C was respectively.

The melting points of the IL decreased as compared to pure drug. The melting point below 100°C, confirms that it is a IL. The change in melting point is due to the combination a cation and anion to form the liquid salt form.

Table 8.4.1: Melting points by capillary method

Sample	Melting point (°C)
Ibuprofen	76 °C
IL	89 °C

8.5 Analytical Method Development of Ionic Liquid

8.5.1 Analytical method-I of Ionic Liquid

Table 8.5.1: Calibration curve observation of Ibuprofen IL in ethanol-water

Sr. No	Concentration (µg/ml)	Absorbance (A)
1	1	0.125
2	2	0.242
3	3	0.347
4	4	0.452
5	5	0.561
6	6	0.69
7	7	0.792
8	8	0.902
9	9	1.015

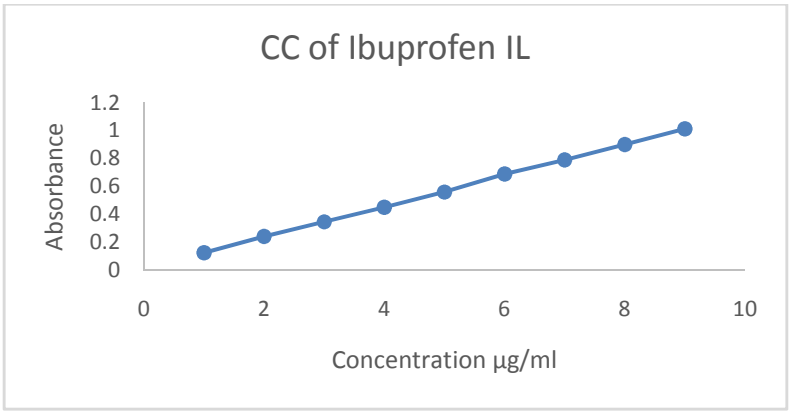

Figure 8.8 : Calibration curve of Ibuprofen IL in ethanol- water

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8.5.2 Analytical Method- II of Ionic Liquid

Table 8.5.2: Calibration curve observation of Ibuprofen IL in 0.1 N HCl

Sr. No	Concentration (µg/ml)	Absorbance (A)
1	10	0.143
2	20	0.279
3	30	0.424
4	40	0.576
5	50	0.730
6	60	0.875
7	70	1.000

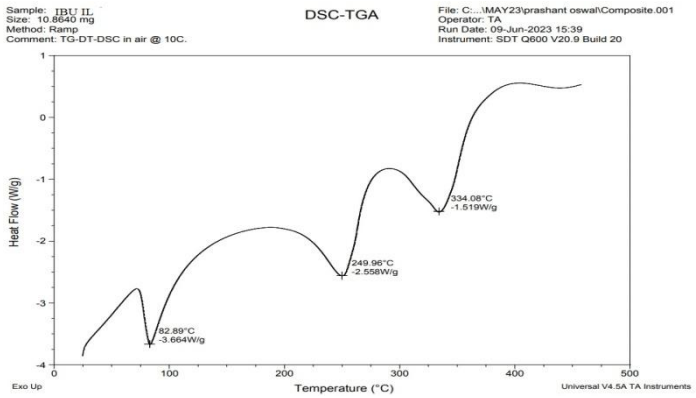

Figure 8.9 : Calibration curve of Ibuprofen IL in 0.1 N HCl

The Ibuprofen- IL was characterized by further methods of characterization.

8.6 Characterization of Ionic Liquid.

8.6.1 DSC

The DSC thermogram of Ibuprofen sodium showed exothermic peak at 80.53°C The thermogram of Ibuprofen IL showed melting point peak at 82.89°C indicating its crystalline nature. This melting point suggests that many new ILs might be readily created by matching a desired cation from such a salt with different anion or vice versa. These type of compounds constitutes “incognito” ILs. All the ILs are also not liquid at room temperature.

8.6.2 IR spectroscopy (IR)

IR spectra of Ibuprofen showed Principle absorption peak at 1457.19 (CH_2 , aliphatic), 1376.06 (CH3,aliphatic), 2954.61 (O-H stretch), 1717.40 (C=0, stretch), 1577.87, 1507.21 (C=C, aromatic stretch).

In the IR spectra of tetra methyl ammonium bromide, principle peaks were seen at 2838.39 (CH_3, stretch), 1486.03 (C-N stretch),1398.84 (C-H asymmetric bend).

IR spectra of Ibuprofen-IL showed principle absorption peaks at 1458.18 (CH_2 , aliphatic), 1377.62 (CH3,aliphatic), 2954 (O-H stretch), 1717.11 (C=0, stretch), 1502.31 (C=C, aromatic stretch). There was shifting of peaks.

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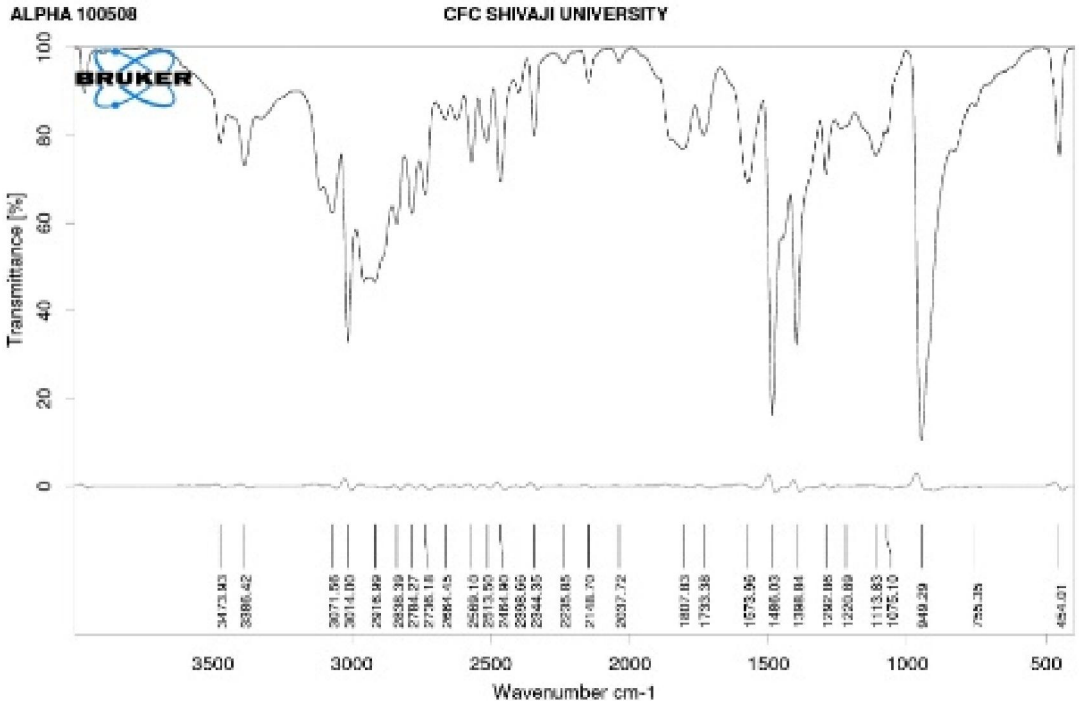

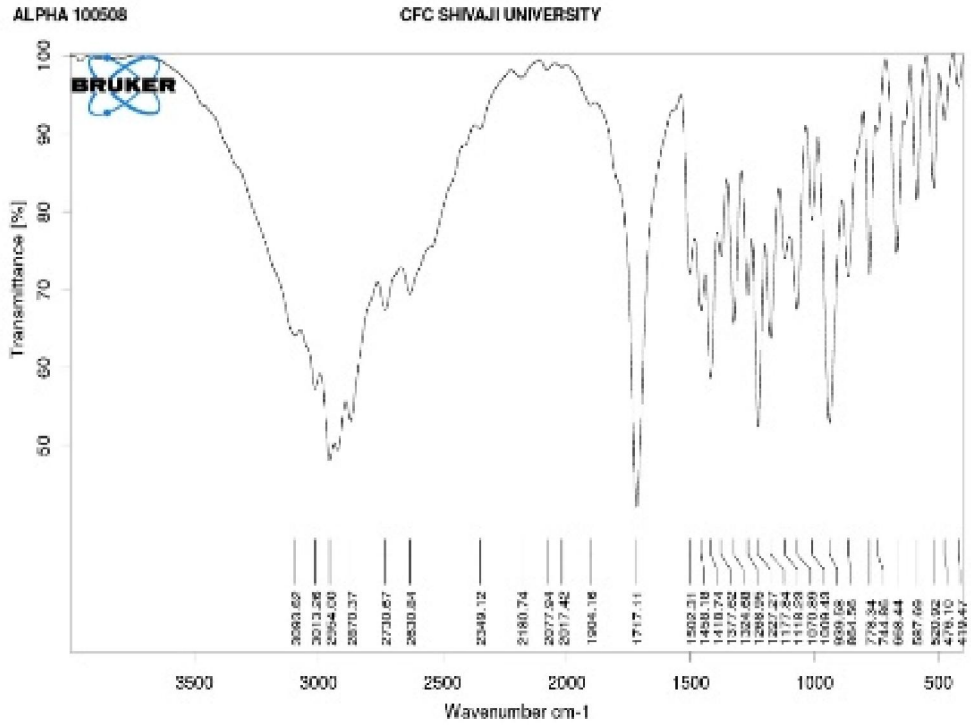

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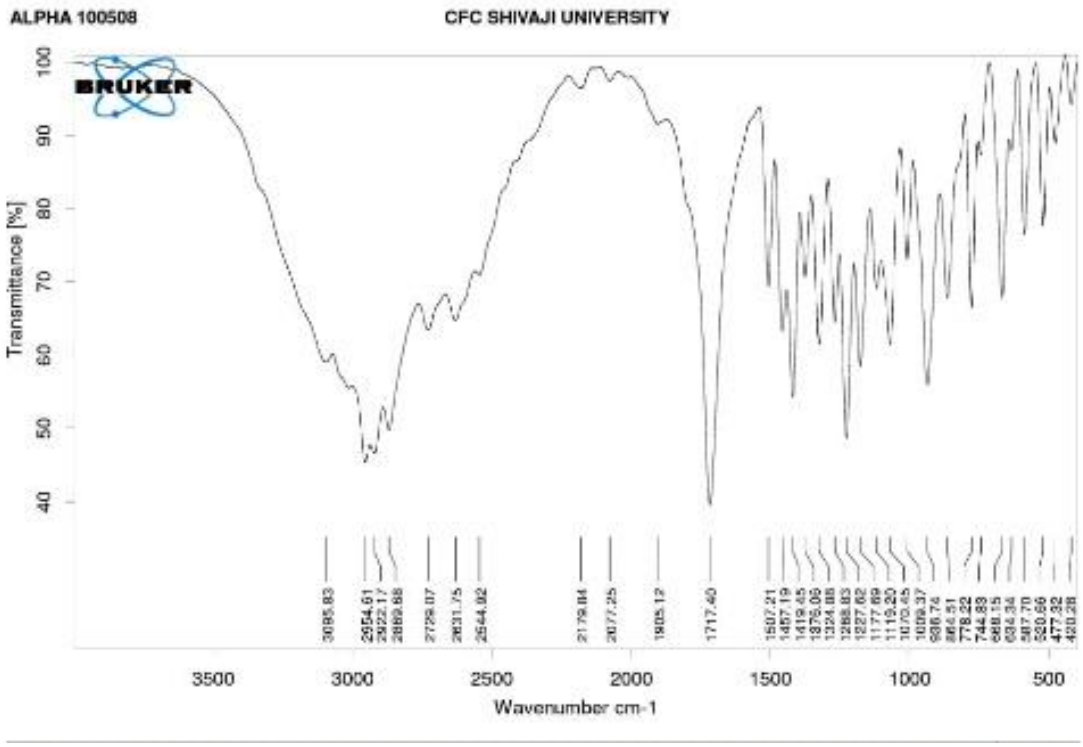

8.6.3 X-Ray Powder Diffraction

The XPRD of Ibuprofen and its IL were obtained. The peaks of XRPD of those compounds with their 2θ angles and intensity are given in table 9.3. The XRPD patterns of all samples are presented in Fig.8.10. The Ibuprofen-ionic liquid showed less intense peaks as compared to the pure Ibuprofen suggesting the phase conversion. The reduction of intensity of peaks of Ibuprofen-ionic liquid indicated the conversion of Ibuprofen into the ionic liquid.

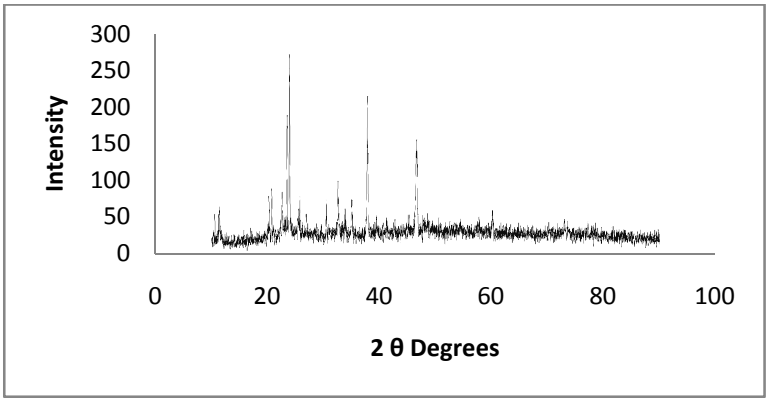

Figure 8.10: XRPD of Ibuprofen-IL

Table 8.6.3: XRPD results showing 2θ values with high peak intensity

Sample	2 Theta (2θ)	Intensity
Ibuprofen	10.8138	81
	15.3010	116
	20.4583	418
	24.3973	149

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	28.5394	269
	31.6459	269
Tetra methyl Ammonium Bromide	10.5295	324
	15.7417	105
	22.5496	1446
	22.6105	1993
	23.4227	628
	27.2805	1489
Ibuprofen Ionic Liquid	10.5295	14
	20.2553	78
	24.0521	69
	30.4886	73
	32.6002	99
	37.8996	214

8.6.4 Saturation solubility studies

The saturation solubility of Ibuprofen, Ibuprofen- ionic liquid was found to be 16.56, 0.1119 respectively. The solubility of Ibuprofen ionic liquid was increased as compared to Ibuprofen sodium.

Table 8.6.4 : Saturation Solubility of Ibuprofen and its IL

Sample	Concentration mg/ml
Ibuprofen	16.56
Ionic Liquid	0.1119

8.6.5 Determination of partition coefficient (log P)

The log Pvalues of Ibuprofen and its ionic liquid were observed to be 2.96 and 0.965 respectively. The decreased log Pvalue indicated the high aqueous solubility of Ibuprofen IL as compared to Ibuprofen.

Table 8.6.5 : Log PValues

Sample	Log Pvalue
Pure Ibuprofen	2.96
Ionic Liquid	0.965

8.6.7 In vitro Dissolution study:

The Ibuprofen release profile by synthesizing its IL is reported in Fig. The release rate profiles were given as the percentage of drug dissolved (vs.) time. The % dissolution efficiency (DE) at 10 min and 40 min was evaluated. The dissolution rate of pure Ibuprofen and its ionic liquid was found to be significantly different. The release rates of IL was increased as compared to Ibuprofen. The conversion of solid form of the drug into Ionic liquid form at low melting point by combination of cation and anion enhanced dissolution profile of ILs.

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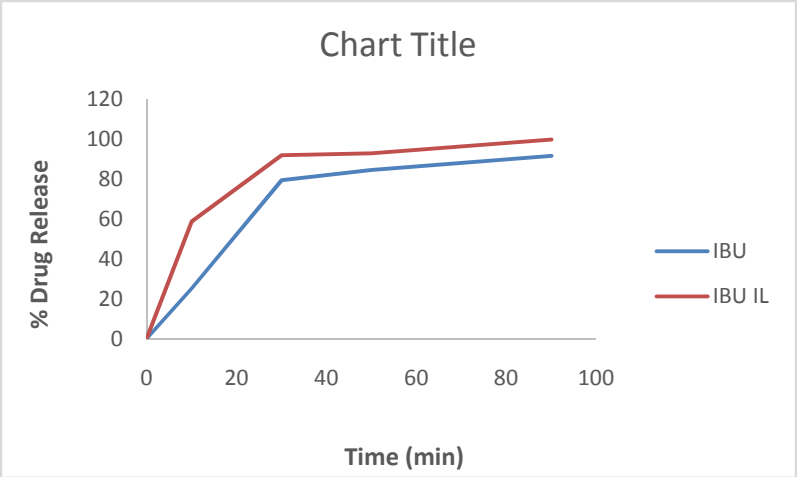

Figure 8.6.6 : Ibuprofen, Ibuprofen IL

Table 8.6.6 : The % drug release and % dissolution efficiency of Ibuprofen and its IL in 0.1N HCl at 37 ± 0.5°C.

System	% DR*				% DE*	
	10 min	30 min	50 min	90 min	10 min	40 min
Ibuprofen	25.18	79.59	84.61	91.73	18.59	47.8
Ibu-IL	58.86	92.04	93.1	99.96	29.43	72.11

IX. SUMMARY & CONCLUSION

Ionic liquids are a promising technique to alter physicochemical properties of the poorly water soluble drugs by judicious combination of cations and anions. API-based Ionic Liquids are synthesized by using API either as cation or anion. API-based ILs was synthesized by combination of cationic Tetramethylammonium bromide and anionic Ibuprofen while pure then ILs. The solid form of the low water soluble API was converted into its liquid salt form to improve physicochemical properties and evaluate biological activity. ILs were synthesized in molar ratios of Tetramethylammonium bromide and anionic Ibuprofen (1:1) The analytical evidences for the formation of ILs were generated and confirmed by differential scanning calorimetry (DSC), Fourier transformation-infrared spectroscopy (FTIR) and X-ray powder diffractometry (XRPD). The solubility and dissolution of 1:1 ILs were significantly improved as compared to Ibuprofen alone, supported by decreased log P values. The improvement of physiochemical properties of IL 1:1 was found to be reliable.

X. FUTURE PERSPECTIVES

- Bioavailability Studies
- Stability Studies
- Toxicity Studies
- Complexes with β-Cyclodextrin in case of ILs with decreased solubility
- Conversion in dosage forms like capsules, gel, etc.

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