Ionic Liquids : Testing the solubility of a NSAID (Ibuprofen) in an ionic liquid

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Summary

Since its invention in 1961, Ibuprofen has been a widely used nonsteroidal anti-inflammatory drug (NSAID) known for its effectiveness in reducing pain, inflammation and fever. It is commonly used to treat conditions such as osteoarthritis, muscle aches, and injuries. Its poor solubility in both water and organic solvents has led to its efficacy in topical applications being limited, as it is not efficiently absorbed by the body via the skin. Those who may not be able to take capsules, such as children and the elderly, have then had to use large amounts of topical ibuprofen for it to be effective, in certain cases leading to skin hypersensitivity.

This prompted us to investigate whether ionic liquids (ILs) may be the solution to delivering Ibuprofen effectively, as they exhibit unique properties of high thermal stability and low volatility in a 'liquid-like' form. In recent years, the use of ILs as drug delivery systems has been a region of substantial development, specifically for poorly soluble medicines. Thus, we framed our research around finding out whether the ionic liquid BMIM-Cl is a suitable solvent for the NSAID Ibuprofen, by comparing its effectiveness as an ibuprofen solvent with both water, and ethanol. We also compared mixtures of solvents, including ethanol/BMIM-Cl; and water/BMIM-Cl.

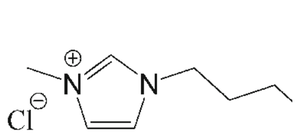
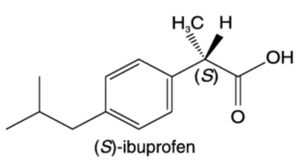


Figure:1 Skeletal structure of BMIM Cl



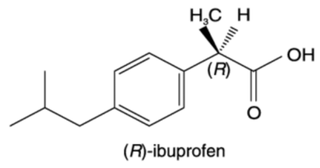


Figure 2: Skeletal structure of the two isomers of ibuprofen

Experimental Method

The solvents tested in this practical are as follows:

- Ethanol
- BMIM-Cl
- A mixture of ethanol and BMIM-Cl (1:1)
- A mixture of water and BMIM-Cl (1:1)

1. Using a micro-syringe, transfer 0.1ml of the solvent to the centre of a watch glass.
2. Crush up an ibuprofen tablet using a pestle and mortar and transfer it into a weighing boat.
3. Place a beaker onto a mass balance and use a spatula to transfer 0.05g of ibuprofen into the beaker.
4. Empty the contents of the beaker onto the watch glass and reweigh the beaker to ensure that the mass of solid transferred was approximately 0.05g.
5. Use a glass rod to finely stir the mixture until the solid dissolves. Time how long this takes.
6. Stop stirring once it appears to the naked eye that the solid has stopped dissolving.
7. Because we used colourless solvents, at this stage we added a few drops of iodine solution to use as a stain and mixed thoroughly.
8. Place the watch glass under the microscope onto its stage and set the objective lens to its lowest magnification.
9. Focus the microscope using the fine and coarse focus knobs, and once focused, increase the magnification of the image to x100 and re-focus the image.
10. Observe and confirm if the solid has entirely dissolved in the solvent.
11. Repeat this procedure using different solvents.

Results

Figure 3: 100% Ethanol

Figure 4: 100% BMIM-Cl

Figure 5: 50% Ethanol 50% BMIM-Cl

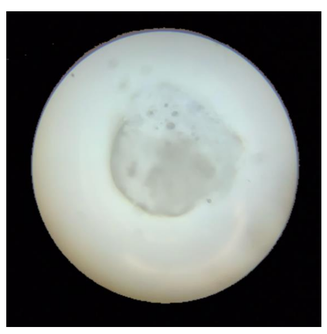
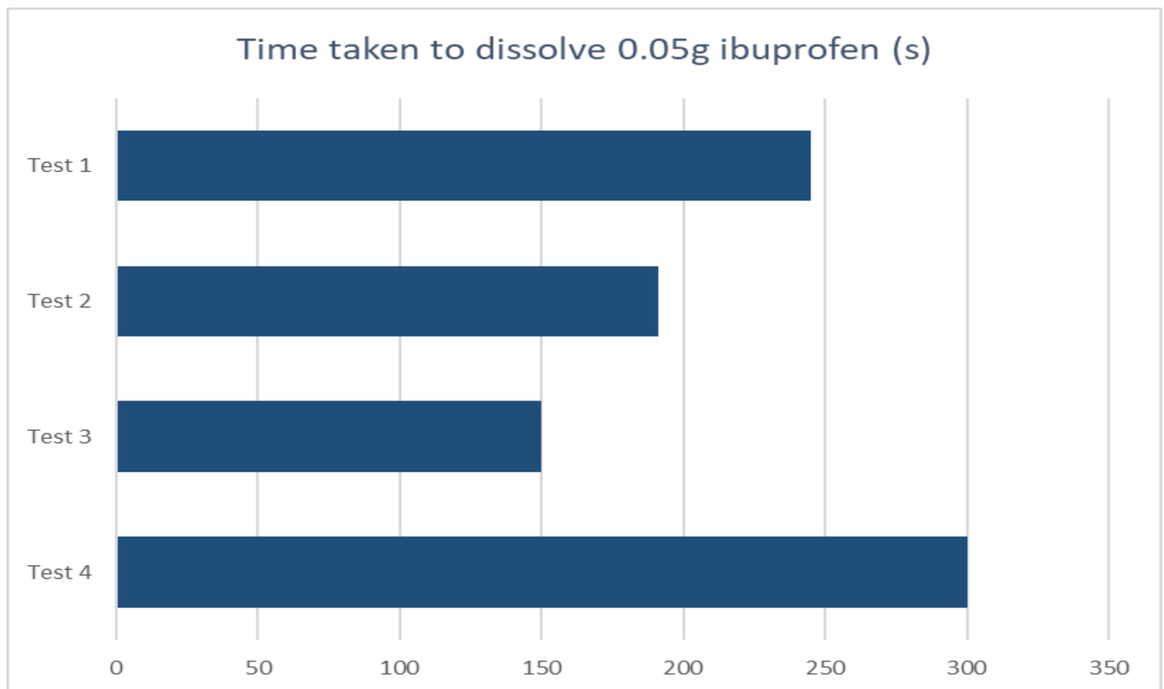


Figure 6: 50% Water 50% BMIM-Cl

Results				
	Ethanol Concentration (%)	Water Concentration (%)	BMIM - Cl Concentration (%)	Time taken to dissolve 0.05g Ibuprofen (s)
Test 1	100	0	0	245
Test 2	0	0	100	191
Test 3	50	0	50	150
Test 4	0	50	50	300



Analysis & conclusions

Based on our research, we have found that using BMIM-Cl as a solvent for ibuprofen is more effective than using ethanol. This was concluded using the images produced by the magnification of our results under a light microscope and comparing each slide to see whether large fragments were present. Photographs of the test samples taken under the microscope show that the ionic liquid BMIM-Cl (see figure 4) worked faster as a solvent for ibuprofen than ethanol. Further trials showed that using a mixture of 1:1 ethanol and BMIM-Cl (see figure 5) was the most efficient at dissolving ibuprofen, as it took the least time to dissolve. Conversely, a mixture of 1:1 water and BMIM-Cl (see figure 6) displayed the largest fragments on the microscopic image and took the longest time to dissolve, making it the worst solvent for ibuprofen . From this we can conclude that using mixture of 1:1 ethanol and BMIM-Cl proved to be the most effective solvent for ibuprofen. This could be a result of the ionic nature of BMIM-Cl which deprotonates the –COOH in both enantiomers of ibuprofen (see figure 2), forming anions which are more soluble in the ionic solution. The addition of ethanol, an organic solvent, to the BMIM-Cl appears to improve the efficacy of the solvent. This may be due to the organic molecule ibuprofen having a stronger affinity for the organic solvent ethanol than it does for water. Further research on the cosolvent effects of ibuprofen and BMIM-Cl would allow us to understand how ibuprofen is able to dissolve more effectively under a 1:1 solution of BMIM-Cl and ethanol.

However, as we only had a small volume of BMIM-Cl available, we were restricted in our ability to repeat the experiment, which caused us to be unable to obtain mean values. This would have increased the validity of our results and would help reduce the effect of any data outliers. Furthermore, having access to an electron microscope would allow us to have greater resolution in our images, as colourless ibuprofen fragments were hard to see under an optical light microscope. This would improve our comparisons (see figure 3-6) and help us further understand whether a BMIM-Cl/ethanol mixture is an effective solvent for ibuprofen.

If we were to build upon our research, we would directly compare propylene glycol with BMIM-Cl as solvents of ibuprofen. Propylene glycol is a non-toxic organic compound, commonly used as a cosmetics ingredient and has previously been used as a base for ibuprofen-containing ointments. However during recent times, it has been associated with irritant and allergic contact dermatitis, and its suitability has been questioned. Thus, efforts have been made to reformulate certain ointments and find new solvents. Our research has shown BMIM-Cl is efficient at dissolving ibuprofen, but further research would help us to specifically investigate its use in topical applications, as this is one of the main forms in which ibuprofen is used with certain demographics such as elderly patients.

References

- Hu, Y., Xing, Y., Yue, H., Chen, T., Diao, Y., Wei, W. and Zhang, S. (2023). Ionic liquids revolutionizing biomedicine: recent advances and emerging opportunities. *Chemical Society Reviews*, [online] 52(20), pp.7262–7293. doi:https://doi.org/10.1039/D3CS00510K.

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