How to make medicines more effective?

Lidia Tajber

Many therapeutic agents – both newly discovered and long existing - lack efficacy because they have difficulty getting to the bloodstream when ingested and cannot therefore reach the required therapeutic destination sites. Typically, the therapeutic agents, also called active pharmaceutical ingredients, that are often given to patients as tablets to swallow must fully disperse into individual molecules following ingestion before being taken up into the circulation, move about the body and show their pharmacological effects.

Nowadays, those active molecules are invented using computer modelling to specifically deal with a given ailment and to have minimum side effects, which means that other properties of those substances, such as solubility (the ability of therapeutic agents to dissolve into a solution containing individual molecules), are often overlooked. It means that the oral medicine (e.g. tablets) will not work effectively or will not work at all. Also, many companies may not engage in development of poorly soluble therapeutic agents due to the enormous costs of transforming such molecules into medicines. Therefore, there is a definite need for smart technological formulation approaches to make drug molecules bioavailable, so the existing and new medication to treat ailments are of the highest efficacy and quality.

Anti-crystal engineering — To address the above problems, my research concentrates on:
— firstly, understanding the origins of poor solubility of active substances,
— secondly, developing a suitable technological strategy to tackle the problem and,
— thirdly, testing the approach using a panel of sophisticated instrumentation and in prototype formulations (simple medicine).

On the first question, why does it happen, the pharmaceutical industry has coined the term “brick dust” for poorly soluble molecules, but often the issue is not with the “bricks” but the “cement”, e.g. the strong bonds that the molecules develop to hold them together in an entity called a crystal.

On the second issue, tackling the problem, breaking the “cement” can be achieved by mixing the crystals with another substance that is able to break the bonds and keep the active molecules separate and readily available for absorption. This approach is called “anti-crystal engineering”. (See Figure 1)

My group in Trinity’s School of Pharmacy and Pharmaceutical Sciences, which is supported by Science Foundation Ireland, aims to develop those multicomponent mixtures, scientifically termed ionic liquids and deep eutectic mixtures, as a viable approach to enhancing bioavailability.

A collaborative approach — On the third issue, testing the approach, we know that critical issues with medicine design can’t be dealt with in isolation, so I have engaged in several networks. Within the Synthesis and Solid State Pharmaceutical Centre (SSPC), a unique collaboration between industry partners and Irish and international academia, my research has mainly concentrated on amorphous (“cement”-devoid) materials for pharmaceutical applications. My group is also involved in two European Commission (EC) supported collaborations:
— the Open Research Biopharmaceutical Internships Support (ORBIS) is composed of six academic partners and four pharmaceutical companies from Poland, Czechia, Finland, Ukraine, Ireland, Germany and the US to advance the current scientific, economic and social challenge of increasing the effectiveness and productivity of drug development processes. The core of ORBIS is the intersectoral and international exchange of researchers working together on solving the problems with medicine development;
— for the project LongActNow, academic partners from Ireland, Germany and a pharmaceutical company based in Belgium will work on injectable long acting medicines.

Lidia Tajber received her MSc Pharm from Medical University of Silesia, Poland, and PhD from Trinity, where she is now an Associate Professor in Pharmaceutics and Pharmaceutical Technology and Director of Research in the School of Pharmacy and Pharmaceutical Sciences. She joined the School in 2007 as a lecturer. Lidia has published nearly 90 peer-reviewed manuscripts and is a co-inventor on patent applications. Her research focuses on fundamental and applied aspects of developing medicines containing poorly soluble drugs.

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Fig 1. Schematic representation of the molecular arrangement of poorly soluble active substance (A) showing the “cement” in grey (top of figure) and comparison between the structures of conventional, solid forms of the active comprising another substance (excipient, E) and the novel, ionic liquid and deep eutectic mixtures, systems.

Neutral molecules

Co-crystal

Deep Eutectic Mixture

Ionised molecules

Solid

Liquid

Salt

Ionic Liquid
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