Novel solid forms of the anti-inflammatory drug oxaprozin may lead to a new combined asthma therapy

November 30 2016

An exploratory study by A*STAR scientists into novel solid forms of the anti-inflammatory drug oxaprozin may lead to improvements for the asthma drug, salbutamol, and help reduce inflammation of the airways.

Many drugs, in their original 'parent' form, are not ideal for use in the human body. For example, poor solubility can limit a drugs' ability to disperse in the bloodstream, as is the case for oxaprozin, a widely used anti-inflammatory. Other drugs dissolve too quickly, lose their potency and require multiple doses, such as salbutamol—a drug used in asthma inhalers to open restricted airways. A solution can be to incorporate two drugs into one solid form to create more effective medications.

"With discoveries of new active pharmaceutical ingredients dwindling, combining two or more ingredients in a single dose is increasingly common for treating complex diseases such as HIV/AIDS and cancer," says Srinivasulu Aitipamula, from the team at the A*STAR Institute of Chemical and Engineering Sciences. "To find a more soluble version of oxaprozin that could be used in solid form, we created five novel crystalline forms of oxaprozin, including three molecular salts made with different organic molecules."

Molecular salts are ionic compounds formed by strong bonding between oppositely charged ions—atoms that have either lost or gained electrons resulting in a positive or negative charge. Aitipamula's team used X-ray

crystal diffraction to determine the crystal structure of each solid and examined the resulting effects on oxaprozin's physical and chemical properties.

While the team did not succeed in altering oxaprozin solubility significantly, one molecular salt incorporating oxaprozin and salbutamol showed great promise for creating an extended-release, anti-inflammatory asthma therapy.

"By incorporating salbutamol and oxaprozin into one solid, we were able to slow the rate of salbutamol dissolution," says Aitipamula. "The solubility of a solid in water depends on the number of hydrogen bonds that it can form with water molecules. All the potential hydrogen bonding sites of salbutamol and oxaprozin were involved in creating the salt, meaning there were no sites left for water to interact with."

The strong crystal lattice in the oxaprozin-salbutamol salt means the molecules are held together firmly, facilitating a controlled release of salbutamol over time. Incorporating oxaprozin into an asthma therapy would also mean patients would no longer have to take supplementary anti-inflammatory drugs. "We will continue to expand our investigations into other active ingredients and create combined formulations for targeting different diseases," says Aitipamula.

More information: Srinivasulu Aitipamula et al. Novel solid forms of oxaprozin: cocrystals and an extended release drug–drug salt of salbutamol, *RSC Adv.* (2016). DOI: 10.1039/c6ra01802e

Provided by Agency for Science, Technology and Research (A*STAR), Singapore