Coumarins show potency as anti-inflammatory drugs

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New methods for the laboratory-scale synthesis of coumarin-based drugs were developed in a recent study completed at the University of Eastern Finland. In his doctoral thesis, Lic. Phil. Juri Timonen also developed new analytical methods for the fast identification of natural and non-natural coumarins. A few of the synthesised coumarins were also found to inhibit some specific reactions generally associated with inflammation.

Coumarin is an aromatic compound, naturally occurring in many plants. In foodstuffs coumarins are found especially in cinnamon and tonka beans. The bioactivity of coumarins has been utilised in many drugs; for example, coumarins exhibit anti-inflammatory as well as anticoagulant activities. One of the best-known drugs based on a coumarin scaffold is Marewan®, a commercial blood anticoagulant.

The study made considerable improvements to the decades-old synthesis method of coumarins. Most of the previous methods are based on heating of the starting material with a strong acid, but the newly developed method also works at room temperature. The improvements also lower the production costs, since the final products are easier to purify.

A commonly used inflammation model showed that some of the synthesised coumarins remarkably reduced the production of typical signalling molecules, such as nitric oxide synthase and nitric oxide itself, which are usually linked to inflammation. In this assay, a murine cell line

from mice imitated the inflammatory response. The results also revealed one of the pathways in which coumarins act. Understanding of this pathway and data on nearly 50 tested coumarins may help in the development of future anti-inflammatory drugs for chronic inflammation diseases such as asthma and rheumatoid arthritis.

Developing new analytical methods for natural and non-natural compounds is important in the screening of natural products with biological activity as well as in studies of drug metabolism. By using a mass spectrometric method developed in this study, even very similar compounds can be distinguished and characterized based on their fragmentation during the analysis.

A fragmentation pattern for a given molecule obtained by a mass spectrometer resembles a fingerprint; it is dependent only on the structure of the molecule and two non-identical molecules produce different patterns. The study revealed some interesting details on the fragmentation of synthesized coumarins. This knowledge can be used in the future to predict fragmentation of novel coumarins.

The findings were originally published in *European Journal of Medical Chemistry*, *European Journal of Mass Spectrometry*, and *Rapid Communications in Mass Spectrometry*.

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