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Chloroform provides clue to 150 year old medical puzzle

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One of the earliest general anaesthetics to be used by the medical profession, chloroform, has shed light on a mystery that's puzzled doctors for more than 150 years – how such anaesthetics actually work.

A discovery described as "true serendipity" made by Leeds University PhD student Dr Yahya Bahnasi, has provided a clue that may unravel the enigma of general anaesthesia – and offer the opportunity to design new generations of anaesthetics without harmful side effects.

"We take general anaesthesia for granted nowadays, but it's still true to say that we don't know exactly how it works on a molecular level," says Dr Bahnasi, a qualified medical doctor on an Egyptian Ministry of Higher Education Scholarship at the University's Faculty of Biological Sciences.

"However, I was examining the relationship between lipids and atherosclerosis [the furring up of arteries] and it just so happened that the lipids I was using were supplied already dissolved in chloroform. I noticed that the chloroform inhibited, or blocked, the calcium ion channel TRPC5 – it was quite a striking effect."

Ion channels are pathways that allow electrically charged atoms to pass across cell membranes to carry out various functions such as pain transmission and the timing of the heart beat. TRPC5 calcium ion channels are found in many tissues around the body but are predominant in the brain.

“We know that this ion channel plays a signalling role in the central nervous system, which regulates the conscious and unconscious states, so I was left wondering whether inhibiting this calcium ion channel was one mechanism by which anaesthesia works,” says Dr Bahnasi.

Dr Bahnasi then carried out further experiments with several other modern anaesthetic compounds, both intravenous and inhaled, and found that the blocking effect on the TRPC5 ion channel was the same.

He says that the discovery opens up the opportunity to design and develop new generations of anaesthetics which directly target TRPC5, but with minimised side effects.

“Of course there are multi-molecular events that work together in anaesthesia, and inhibiting the TRPC5 ion channel may just be one of them. But it’s a great start in piecing together the underlying mechanisms and providing a novel molecular target for new drug design,” he says. “And it’s particularly fitting that this evidence was revealed by chloroform, the ‘grandfather’ of modern anaesthetics.”

Source: University of Leeds