

Vicks VapoRub shows its speed

Professor Ron Eccles
Dr David Hull



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Vicks VapoRub (VVR) has been commercially available for over 100 years, as a remedy for congested nasal passages. A study led by **Professor Ron Eccles and Dr David Hull** has now demonstrated the speed of its effect in common cold sufferers.

To begin, what attracted you to this area of research?

Professor Ron Eccles: During my modular zoology undergraduate course at Liverpool University, I chose to do a module in pharmacology. I found the investigation of how drugs work in humans an amazing and exciting area of study and decided to switch my undergraduate studies to pharmacology. I was lucky enough to be offered a PhD scholarship after completing my undergraduate studies, and I chose to study the pharmacology of the nose, as I could see this was a very under-researched area. I fell in love with the nose during my research as there were always more questions than answers in this area, and I felt that I could contribute to knowledge in this area. When I got my first job at Cardiff University, I continued with nasal research and found a problem that did not seem to have an answer. How does menthol work on the nose to provide relief from nasal congestion? Menthol was an ingredient in a lot of Vicks products such as their 'Vaporub', inhalers and nasal sprays, but when I looked at the chemical formula for menthol it did not have any of the properties of a drug that would work as a nasal decongestant by constricting nasal blood vessels. I wrote to the Richardson Vicks Company based near London, UK in 1976 expressing my interest in the mechanism of action of menthol, and after several years of discussion and meetings I got the first of many research grants to study this mechanism.

The formula for VVR was developed over 120 years ago and is one of the most well-established household cold remedies. Why perform this study now?

Dr David Hull: We continue to explore the attributes of all products, young and old. As ideas, and sometimes new methods emerge, we strive to bring this to bear by gathering an improved understanding of their effects. We knew that VapoRub was fast-acting (just open the jar and you can feel an effect), but we had not tried to quantify that before and we did not know if the feeling extended from just cooling to an actual sense of decongestion. In conversations with our internal experts, we concluded that this would be worthwhile testing so that we could obtain a clear appreciation of 'just how fast' VapoRub is.

Furthermore, we know that there isn't a great deal of awareness of the clinical efficacy studies of VapoRub amongst healthcare professionals so we recognised this as an opportunity to build on our clinical knowledge.

Do you anticipate the results of this study strengthening sales of VVR? Or is there a strong separation between R&D and marketing at Procter and Gamble?

Dr David Hull: We in R&D always hope that our work will support the commercial success of our products. We believe that effective communication to healthcare professionals and patients is crucial to this, so we would expect these results to be valuable to our colleagues in Marketing as they communicate with both constituencies.

Besides potentially improved sales of VVR, what is the wider impact of this research?

Dr David Hull: I believe that the results of this study affirm the place of aromatic oils

in the treatment of upper respiratory tract infections such as the common cold and flu. Since science came to understand the receptor biochemistry of these substances, the exploration of their effects has been more easily explained. Also as we now have a receptor-based pharmacology for aromatic oils to work with, we can better plan experiments such as this one in the expectation of an interesting and valuable result.

Did they get it exactly right with the original formula or do you think it can be improved? What else does the future hold for this product?

Dr David Hull: Well, I must begin by complimenting Mr Richardson, who developed such a clinically valuable therapy presumably by trial and error back in the 1890s. Is it beyond improvement? I doubt it. We continue to explore possibilities for this product and as we find new information we will be bringing it to the public domain. As most of our work is proprietary, I think my answer has to be 'watch this space'!

Are there plans for future studies into VVR efficacy?

Dr David Hull: We continue to listen to the patients who use our products and explore new science as it emerges to guide our work. We will therefore continue to look at Vaporub to see if we can understand better the benefits that it provides. If new ideas emerge, then we will test them.



MEASURING HOW RAPIDLY VICKS VAPORUB EXERTS ITS PHARMACOLOGY

Researchers at the Common Cold and Nasal Research Centre at Cardiff University, in collaboration with PGT Healthcare, a joint venture between the Procter and Gamble Company and Teva Pharmaceuticals, have investigated the speed of nasal cooling and decongestion of Vicks Vaporub in common cold sufferers.

The history of Vicks Vaporub

Vicks VapoRub (VVR), was developed in North Carolina in the 1890s. It quickly established itself as one of the best-selling cold remedies at the time and has remained a household staple ever since. With half a million Facebook 'likes', availability in over 60 countries, worldwide production in excess one million gallons per year and sales totalling over one billion units in the last five years alone, the popularity of Vicks appears unshakeable.

The original formulation was created by Greensboro pharmacist, Lunsford Richardson who purportedly borrowed the name 'Vick' from his brother-in-law, Dr Joshua Vick, because it sounded snappier than Richardson. Though he concocted various other remedies such as Vick's Chill Tonic, Vick's Little Laxative Pills and Vick's Tar Heel Sarsaparilla, nothing quite compared to the success and popularity enjoyed by VapoRub.

Richardson's death in 1919 resulted rather ironically, from the Spanish flu pandemic which had propelled VapoRub sales from \$900,000 to \$2.9 million in a single year. The company he founded, Richardson-Vicks, was bought by Procter and Gamble (P&G) in 1985.

'After decades of research we now know that menthol acts on TRPM8 sensory nerve receptors in the nose to cause a cool clear sensation of nasal airflow and this is the basis of its action in providing relief from nasal decongestion.'

R&D at P&G

P&G have conducted various studies into the efficacy of VVR for cold and flu relief, demonstrating that it reduces cough frequency relieves nasal congestion and lasts up to eight hours. Their most recent study, published in the Open Journal of Respiratory

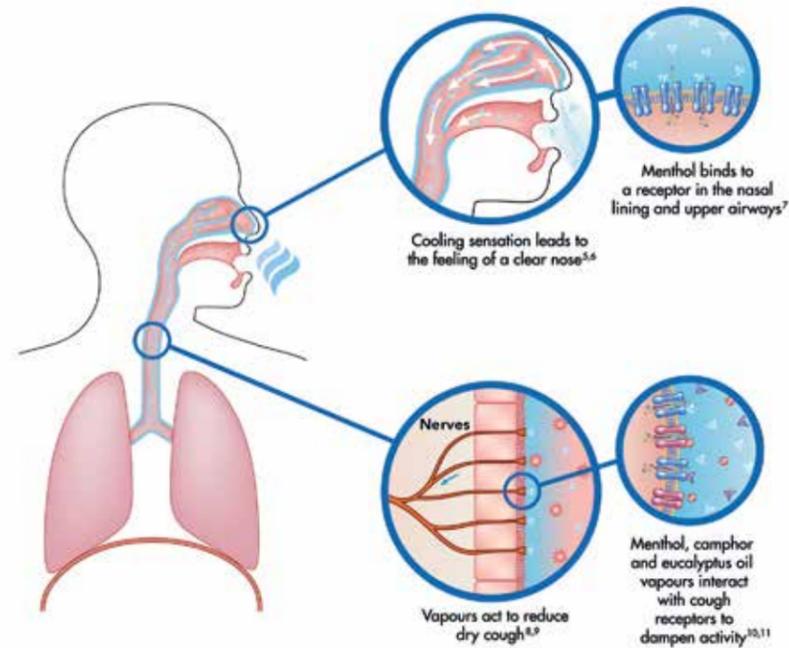


Diseases in collaboration with researchers at the Common Cold and Nasal Research Centre at Cardiff University, focussed on the speed of action of VVR, compared to a petrolatum control using a group of 50 common-cold sufferers. Cold and flu sufferers report that one of the main desires for any medication is a feeling of rapid relief from nasal congestion, as this symptom interferes with day to day activities, can prevent sleep and is generally uncomfortable.

The results showed that VVR produces nasal cooling and congestion relief significantly more rapidly than the control, though after a longer period of time, the petrolatum control was also reported to produce these effects. In the treatment group, VVR produced a sensation of nasal cooling around 23 seconds after application (around 99 seconds for the control), while nasal decongestion was achieved after around 62 seconds (126 seconds for the control). When asked about this placebo effect, David explains, 'In one sense, if we had not seen a placebo effect we would have doubted our results. All medical treatments and procedures are subject to this effect. The question is whether we can account for it satisfactorily. The difference observed provides confidence that the VapoRub mediated effect was clinically more significant.'

Blinding an odour

Their study was single-blind (blinded to the investigators only), due to the nature of the product. The distinctive odour of VVR is inextricably linked to its activity, so the patient will immediately know whether they are in the control or treatment group, once



their nose clips are removed following application. The nose clips were worn in order to standardise the start time of the inhalation process, though the investigators' nose clips remained on for the duration of the experiment. The participants were instructed to stop two clocks which were started when the nose clips were removed, the first one upon the sensation of nasal cooling and the other upon experiencing nasal decongestion. The expectation of these two events may have been a strong factor in the observed placebo effect in the control group.

The researchers also suggest that the placebo effect could have been exaggerated within the control group resulting from the way the nose clips were used in the study. The clips were applied to patients before entering the study area and remained on during the application of the product. This inevitably means that the patients are mouth-breathing, and there is no airflow through the nose during this period. Upon removal of the clips, the control group may have experienced the sensation of nasal cooling, not as an effect of the petrolatum, but resulting solely from the removal of nose clips after wearing them for 3–5 minutes. 'There is no getting away from the placebo effect,' says David, 'the trick is to design the study such that the performance of the active product can be reliably assessed. This study design achieved that.'

The pharmacology of Vicks

There is a scientific explanation behind the activity of VWR, largely based on the interaction between the vaporised active ingredients and receptors found within the sinuses. VWR is paraffin-based and contains levomenthol, eucalyptus oil, turpentine oil and camphor as its active ingredients. These are inhaled when applied topically to the chest and throat, and are evaporated by body temperature, or if added to hot water.

The menthol and eucalyptus oil in the formulation interact with a

receptor located within sensory neurons in the nose which are also responsible for the detection of cold temperatures. This interaction causes the sensation of nasal cooling, feeling similar to breathing cold air through the nose. The nature of this interaction was not elucidated overnight. 'Studies on the D- and L-stereoisomers of menthol lead me to believe that menthol works on a very specific receptor in the nose, as the L-isomer gave relief from nasal decongestion but the D-isomer was inactive,' explains Ron, 'after decades of research, we now know that menthol acts on TRPM8 (also known as CMR1 – cold and menthol receptor 1) sensory nerve receptors in the nose to cause a cool clear sensation of nasal airflow, and this is the basis of its action in providing relief from nasal congestion.'

Other uses and the future of Vicks

A difficult-to-test concept for a future study would be to investigate the efficacy and speed of action of VWR specifically on coughing, a symptom which VWR is widely accepted to provide relief from. This is harder to investigate however, due to the sporadic nature of coughing. This would arguably be even more subject to the placebo effect, as coughing is often a conscious decision. A study performed on children with upper respiratory tract infections did show that an application of VapoRub caused reduced nocturnal coughing, nasal congestion and sleep difficulty, based on surveys completed by their parents. This symptomatic relief also allowed the parents to get a better night's sleep themselves.

The results of the current study may help to reinforce to healthcare professionals that Vicks VapoRub should not be grouped into the long list of over-the-counter cough and cold remedies with dubious efficacy, as it actually has rapid and measurable effects. When asked what the future holds for Vicks, David says, 'watch this space!'

PROFESSOR RON ECCLES & DR DAVID HULL



Meet the researchers

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Ron studied pharmacology at Liverpool University before specialising in the pharmacology of the nose during his PhD studies. He continued his research in this area at Cardiff University, and began working with Richardson Vicks in 1976, studying the pharmacological activity of menthol.

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David is a molecular virologist who originally studied the role of viral genetics in the assembly of viral particles. His PhD studies at Queen's University in Belfast were focused on the measles virus, which he then continued to study at Rockefeller University in New York. He later researched the influenza virus at Northwestern University, Chicago, before joining Procter and Gamble to investigate the pathophysiology of upper respiratory tract infections and the efficacy of non-prescription remedies.

After 30 years' experience in science, he has recently gone 'back to school' in his spare time, achieving a 1st class BA (Hons) in Philosophy and Religious Studies from the Open University in 2011 and an MA in Philosophy in 2015.

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