With a slip under the tongue, allergy tablets subdue the sniffles

Thanks to an unusually mild winter, spring allergy season is already in full swing in the US, which means countless cases of sniffling, sneezing and watery eyes. Antihistamines and steroids can provide cheap and safe relief for the more than 35 million Americans who suffer from pollen allergies. But these medicines wear off quickly, and the allergy injections that confer longer lasting results are painful, inconvenient and carry a risk of life-threatening anaphylactic reactions. "A lot more people will be willing to take a therapeutic approach that is safer and easier to administer," notes Peter Creticos, an immunologist at the Johns Hopkins Asthma and Allergy Center in Baltimore.

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Grass roots medicine: Allergy tablets containing grass and other pollens are nearing the US market.

Enter the allergy tablet. After six years of sales in Europe, these 'sublingual immunotherapy' drugs, which can be dissolved under the tongue to provide long-term allergy relief without the pain of a shot, are finally nearing approval in the US. At last month's American Academy of Allergy, Asthma & Immunology annual meeting in Orlando, Florida, Creticos reported results from a 565-person phase 3 North American study showing that a ragweed allergen tablet being developed by the pharmaceutical giant Merck reduced allergy symptoms by 21–27%, depending on dose, compared to dummy tablets.

At the same time, Creticos and his colleagues reported the findings of two late-stage trials involving another Merck tablet, this one for allergies to Timothy grass. In those studies, which included almost 800 children and adults, the experimental grass allergen tablet yielded similar improvements in nose and eye symptoms over the course of a year.

The efficacy of both drugs, which work by sensitizing individuals to their allergens, was only slightly below the 35% average improvement typically observed for allergy injections. And, importantly, both had only minor side effects, such as mouth itchiness and throat irritation. According to Rupert Vessey, head of respiratory and immunology research at Merck, the New Jersey–based company plans to submit both products for US regulatory approval in 2013.

The US prescription allergy drug market is estimated to reach $15 billion by 2015, according to Global Industry Analysts, a California-based market research firm, and many other companies are similarly hoping to cash in with sublingual immunotherapies, too. For example, North Carolina–based Greer Laboratories currently has an ongoing phase 3 study testing ragweed pollen extract administered under the tongue, and the company has completed phase 1 studies for dust mite, Timothy grass and cat hair tablets. Meanwhile, the French firm Stallergenes, Europe's second largest maker of allergy medicines, completed a US phase 3 trial for a five-grass pollen allergy tablet called Oralair in 2010.

Mixing it up

Should these companies' drugs hit the market, allergy sufferers, the majority of whom are sensitive to multiple allergens, may have to take several tablets concurrently. Yet that could compromise their efficacy, given data reported in January showing that sublingual treatment for multiple allergens might not work as well as single-allergen treatments (*J. Allergy Clin. Immunol.* doi:10.1016/j.jaci.2011.11.019, 2012). In that case, allergy shots, which can bundle a number of allergens into a single injection, may still be the best option for some people, notes Ketan Desai, founder and chief executive of International Medical Consultants in Easton, Pennsylvania.

What's more, allergy shots might provide more durable control of symptoms than under-the-tongue tablets—although promising long-term data for sublingual products is starting to come out of Europe. In January, for instance, a team led by Stephen Durham, head of allergy and clinical immunology at the UK National Heart & Lung Institute in London, reported the results of a five-year study involving Grazax, the same grass tablet tested by Merck and currently marketed in Europe by Denmark's ALK-Abelló. When subjects stopped taking the tablets after three years of treatment, they maintained a reduction in symptoms for two years, the researchers found (*J. Allergy Clin. Immunol.* **129**, 717–725, 2012).

"There's no question that, just like the shots, after three years of treating a pollen allergy you see benefits that persist for a number of years," says Harold Nelson of the National Jewish Health Hospital in Denver, who led Merck's US grass tablet study but was not involved in the European trial.

Ultimately, without more studies across various patient groups, "it is difficult to determine who would most benefit from sublingual immunotherapy," notes Wesley Burks, a pediatric allergist at the University of North Carolina School of Medicine in Chapel Hill who was not involved in the tablet trials but consults for Merck and Greer on food allergy research. "But, clearly, more people would be able to undergo allergy immunotherapy than do now."

Megan Scudellari

Corrections

In the March 2012 'Biomedical Briefing' (*Nat. Med.* **18**, 336–337, 2012), Marc Scheetz's last name was misspelled as Sheetz. The error has been corrected in the HTML and PDF versions of the article.

The last sentence of the interview, 'Straight talk with... Robert Beall' (*Nat. Med.* **18**, 335, 2012), did not appear in its full form in the print version of the March issue. The last line of Beall's response to a question about charities adopting a venture philanthropy approach should have been: "The fact is that many of these boards are seeing what's happened to the CF Foundation and are saying, 'Why don't we do that?'" The sentence was always correct in the HTML and PDF versions.