

Hazardous chemicals from cigarette flavourings identified in tobacco smoke

A new study in the United States shows that smokers inhale hazardous chemicals that originate from compounds used to flavour cigarettes from tobacco smoke (*Journal of Agricultural Chemistry*, 2000, **48**: 1298–1306). Flavourings are used in certain brands of cigarettes to enhance the taste experienced by smokers. The tobacco industry declares that most of the additives it uses are “generally recognized as safe”. However, most flavour additives tested are classified as safe when they enter the human body through the ingestion of food and not through inhalation. Moreover, flavour-related compounds present in cigarette tobacco are transformed by burning cigarette coal to alkenylbenzenes. Combustion products of additives are not safe simply because the original materials are classified as being without risk.

For the first time, scientists have now measured flavour-related alkenylbenzenes in tobacco smoke particulate by a very sensitive method (selected ion monitoring gas chromatography–mass spectrometry). In the past, the measurement of flavour-derived alkenylbenzenes required as much as 1 kg of smoke condensate, which is equivalent to the smoke from 50 000 cigarettes. Stephen B. Stanfill and David L. Ashley from the Centers for Disease Control and Prevention, Atlanta, Georgia, USA have developed a method than can detect alkenylbenzenes in the mainstream smoke particulate of a single cigarette in the low nanogram range. The findings are not only important in understanding the composition of tobacco smoke, but will also be useful in showing if these compounds have a role in smoking-related pathology after repetitive long-term inhalation.

Five alkenylbenzene compounds were identified and quantified in the smoke particulate from eight brands of cigarettes currently on the market in the United States. The brands had mean levels of alkenylbenzenes in the range 6.6–4210 ng per cigarette. The complete blocking of ventilation holes in the cigarette filter increased the transfer of alkenylbenzenes from tobacco to the particulate fraction of mainstream smoke 2–7-fold. Over a 30-year period, a two-pack-

a-day smoker who is exposed to a seemingly small amount of alkenylbenzenes on a per cigarette basis, could inhale up to milligram amounts of alkenylbenzenes from smoke particulate alone.

Research data on the acute toxic properties of alkenylbenzenes are available. For methyleugenol, carcinogenic and mutagenic effects have been demonstrated in rodents; for myristicin and elemicin, genotoxic and hallucinogenic effects have also been established.

Dr John Slade, Head of the Program in Addictions at the University of Medicine and Dentistry of New Jersey, New Brunswick, NJ, said that these results “point to some of the information that regulatory agencies should require cigarette makers to divulge: what are all the desired functions that each additive and its combustion products play in manufactured cigarettes and what is known about adverse effects or potential toxicities of each additive and its combustion products in manufactured cigarettes? He added: “Regulatory agencies need to understand these products well enough to regulate them intelligently.” ■

Tudor Toma, *London*

Oral AIDS vaccine to be tested in the Republic of Uganda

Researchers at the Institute of Human Virology in Baltimore have announced plans to begin human tests of an oral vaccine for acquired immunodeficiency syndrome (AIDS). The vaccine is produced by an innovative approach that uses engineered salmonella bacteria to deliver genetic material encoding vaccine DNA to human cells.

The vaccine is being developed at the Institute of Human Virology at the University of Maryland headed by virologist Robert Gallo. Although Gallo himself cautioned that the vaccine is still untested in humans, Dr. Francis Omaswa, Uganda’s Director of Health Services, said plans are already set for the first clinical trials. The trials, which will be conducted on volunteers, could begin within 18 months.

Uganda is the only African nation to implement aggressively a significant range of AIDS prevention services. 1.5 million people in Uganda are already infected with the AIDS virus, and more than a million chil-

dren have already become orphans as a result of the epidemic. Recently, a new international forum to promote the development of an AIDS vaccine was announced by the World Health Organization (WHO) and the Joint United Nations Program on HIV/AIDS (UNAIDS). In a statement issued in Geneva, the forum stated that the HIV Vaccine Initiative aims to increase international cooperation in the development of AIDS vaccines in the face of the epidemic’s rapid spread in developing countries. The forum’s coordinator, Jose Esparza, said the large number of HIV strains and the number of potential vaccines being tested made it imperative to coordinate research efforts.

The AIDS vaccine being developed by Gallo’s team is the first designed to be taken orally as a pill. In contrast with vaccines that must be injected, the pills would be inexpensive to manufacture and easy to distribute widely. They would also be easily and safely administered by community health care workers, who would need little or no medical training.

Dr. Anthony Fauci, one of the US government’s leading AIDS researchers and Director of the National Institute of Allergy and Infectious Diseases, said that the vaccine developed by Gallo’s team is “theoretically the right approach.” But, like Gallo, he warned, “We’ve been fooled so many times about new vaccines that I’ve hesitated to talk about this one until now, but I really like it.”

Development of the vaccine at the Institute of Human Virology at the University of Maryland is being supported by a 4-year-old not-for-profit organization called the International AIDS Vaccine Initiative. The initiative — which is largely funded by the Rockefeller Foundation, the William H Gates Foundation and other UN agencies — engages in what it calls “social venture capitalism.” Money is funneled to researchers who guarantee that their vaccines, if successful, will be produced cheaply and be readily available to developing countries.

Although many drug companies have developed potential AIDS vaccines, neither they nor federal agencies have earmarked a significant part of their research money for testing in clinical trials. None has focused on an oral vaccine, and only one, AIDSVAX,

of the other 28 AIDS vaccines that have been clinically tested in the United States and around the world has shown any real promise. AIDSVAX is made by VaxGen, a Brisbane-based biotechnology firm that first began developing it more than 15 years ago. It is currently in the final phase of human testing in Thailand and in several American cities.

Dr. George Lewis, Vaccine Research Director at the Institute of Human Virology, said it has taken six years to develop the oral AIDS vaccine, but now "we want to make sure it moves into the field as fast as possible." The DNA vaccine is designed to pass through the intestinal tract and reach particularly vulnerable targets, among them the rectum and the vagina. The viral material in the vaccine would then trigger mucosal immunity as opposed to the cellular immunity that most other AIDS vaccines are designed to induce.

The new oral vaccine should cost less than US\$ 1 per dose, according to the leaders of the AIDS Vaccine Initiative, which has committed at least US\$ 3 million over the next three years for the testing programme in Uganda. Since the onset of the global AIDS epidemic, scientists have watched helplessly as the virus continues to mutate and today there are many different strains in different regions of the world. Gallo said, the Uganda vaccine, if it proves effective, would only combat the HIV strains prevalent in East Africa. However, segments of other HIV genes from strains isolated from other parts of Africa, or from India and Southeast Asia as well, could be readily spliced into the salmonella genome to target populations in those regions.

Despite the introduction of many powerful drugs against AIDS, a vaccine is widely seen as the only way to stem a pandemic in which about 35 million people have been infected worldwide. The drugs, which fight the virus once it has taken hold, cost many thousands of dollars, well beyond the means of people in developing nations where most of the cases occur. The effort to develop these vaccines will be aided by the HIV Vaccine Initiative, which will focus on strengthening the capacity of poorer countries to continue to hold vaccine trials.

Barry Bloom, Dean of the Harvard School of Public Health and head of the new forum's advisory committee said: "We are fortunate that new initiatives are being proposed to expand availability of existing vaccines in developing countries and to conduct research to develop new ones". ■

Scott Gottlieb, *New York*

UNAIDS estimates that half the teenagers in some African countries will die of AIDS

A new report issued by the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that the AIDS epidemic may kill up to half of the young adult population in African countries where the disease has the highest prevalence. *The Report on the Global HIV/AIDS epidemic: June 2000* summarizes the current level of the AIDS epidemic worldwide at the start of the 21st century.

The figures for Africa are alarming and devastating effects on society are predicted. In addition to immediate health care problems, the epidemic threatens to destroy national development, increase inequalities between advantaged and less-advantaged members of the population, and have a negative impact on education. According to the report, South Africa has the largest number of people living with HIV/AIDS in the world, estimated at 4.2 million infected people. In 16 African countries, more than one tenth of the adult population is infected with the human immunodeficiency virus; in seven countries in southern Africa, at least 20% of the adult population is living with the virus.

Only in a few African countries are there signs of some progress. Uganda has brought its estimated prevalence rate down to around 8% from a peak close to 14% in the early 1990s with strong prevention campaigns. A large increase in condom usage has contributed to the lower rates of infection.

18.8 million people worldwide have died from AIDS since the beginning of the epidemic, 3.8 million of them children. About 34.3 million are estimated to be living with the virus. The report is available via the Internet at http://www.unaids.org/epidemic_update/index.html ■

Barry Whyte, *Bulletin*