

Snowdrops: the heralds of spring and a modern drug for Alzheimer's disease

In this article, **Michael Heinrich** looks at how galantamine came to be used to treat Alzheimer's disease

During the darkest days of the year, when nature seems to be asleep, waiting for the brightness of spring brings back memories of times past, most notably, of one's childhood.

In some people, however, memories, particularly of the immediate past, are distorted because of dementia. According to the Alzheimer's Association, approximately two-thirds of all cases of dementia in the elderly are caused by Alzheimer's disease. Alzheimer's disease is a neurodegenerative disorder affecting major brain areas, such as the cortex and limbic system. It often begins with symptoms like short-term memory loss, but it is not just memory that is affected. The disease continues with more widespread cognitive and emotional dysfunction, resulting in substantial and long-lasting disability over the approximate seven to 10 years from diagnosis to eventual death. Although Alzheimer's disease usually has no effect on motor or sensory functions, some atypical clinical presentations (eg, spastic paraparesis) are occasionally found.

Alzheimer's disease generally affects 3 per cent of people aged 65–74 years, 19 per cent of those aged 75–84 years and 47 per cent of those aged 85 years and over. According to the World Health Organization, around 35 million people in industrialised countries will suffer from Alzheimer's disease by 2010, the number of patients rising with increasing life expectancy.

Why touch on such a depressing topic during this festive period? There is a surprising link between a treatment for this debilitating disease and our waiting for the first ambassadors of spring: snowdrops. Galantamine, a medicine used today to treat Alzheimer's disease, occurs naturally in several members of the amaryllis family (Amaryllidaceae). The alkaloid was first isolated from snowdrop (*Galanthus* spp, most notably *G woronowii*). The idea for developing a drug from these species seems to be based on the local use of one of them in a remote part of Europe. Today, galantamine is obtained from other members of the same plant family, like daffodil (*Narcissus* spp) and snowflake (*Leucojum* spp), as well as being made synthetically.

Galanthus species are native to many parts of Europe including the south-eastern European countries, the eastern parts of Turkey and the Caucasus mountain range but, overall, little has been published about the use of galantamine.

Ethnopharmacology

The study of local and traditional knowledge is an area of scientific enquiry today commonly called ethnobiology. If the knowledge relates specifically to medicinal plants, the subject is called ethnopharmacology. As a specifically labelled field of research, ethnopharmacology has had a relatively short history. The term was first used in 1967, in the title of a book on hallucinogens: 'Ethnopharmacologic search for psychoactive drugs'. However, the concept of developing drugs from plants used in traditional and local medical systems is much older and broader.

Information about such use is based on a researcher living in a community, introducing the people to his or her research interests, eating their food and sharing their joys and fears. The goal of such research may well be to find new drugs but, often, the ethnopharmacologist is more interested in the local development of these resources. This kind of research is, generally, hypothesis driven and based on a series of well-established field and laboratory methods. It is often conducted in tropical countries, but may well be conducted in temperate regions of the world.¹

Although in some cases, direct links between a local and a biomedical use exist, in others the relationship is more complex. All too often our information about such local or traditional use is limited. In the case of galantamine, we are faced with a difficult detective story, which leaves us with many unresolved riddles.

Traditional use of galantamine

Little sound evidence for the traditional use of the *Galanthus* species exists. Snowdrop was possibly used in ancient Greece. In 1983, Plaitakis and Duvoisin hypothesised that that Homer's "moly" might have been the snowdrop (*G nivalis*).² In his epic poem, *The Odyssey*, Homer described moly and its use by Odysseus as an antidote against Circe's poisonous drugs. Thus the Greek description of moly might represent the oldest recorded use of *Galanthus*, but the evidence is scanty. Jumping to the 16th century and to the classical medico-botanical texts of the renaissance (ie, by Fuchs, Bock, Brunfels, Turner and Gerard), we note that they do not mention *G nivalis*. In Köhler's 'Arzneipflanzen' of 1889,

Michael Heinrich is professor of pharmacognosy at the Centre for Pharmacognosy and Phytotherapy, School of Pharmacy, University of London

Correction

There was a mistake in the chemical structure of galanthamine as originally printed. The correct structure is shown below.

