	Experiment title: Weizmann Institute of Science Structural Biology (WIS-SB)BAG	**Experiment number**: LS-1680
Beamline: ID14-2	**Date of experiment**: from: May 11 2000 to: May 12 2000	**Date of report**: July 25 2005
Shifts: 3	**Local contact(s)**: Ed Mitchell	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

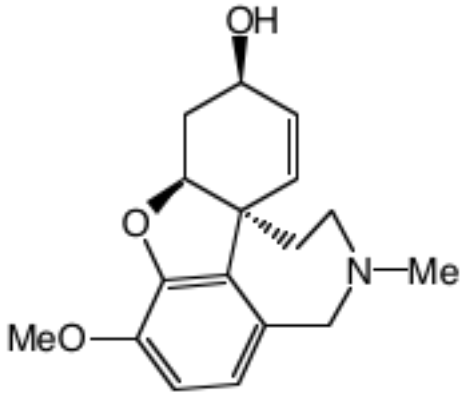
***Harry M. Greenblatt Dept. of Structural Biology, Weizmann Institute**

Report:

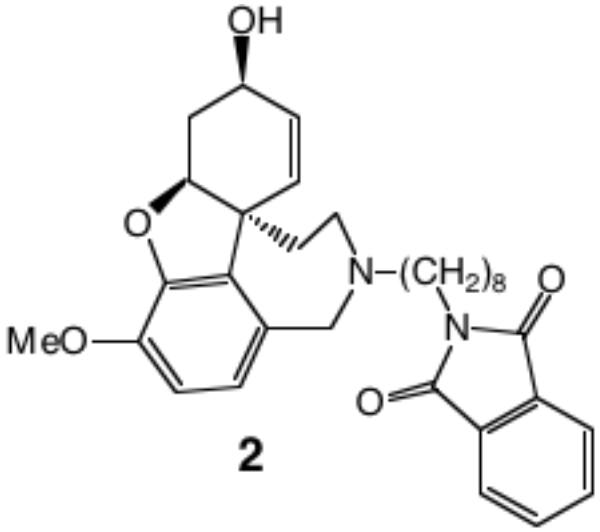
One of the apparent causes of memory loss in Alzheimer's disease is due to cholinergic insufficiency. Thus, in cholinergic synapses, too little of the neurotransmitter acetylcholine (ACh) is released into the synaptic gap, and signal transmission is impaired. Acetylcholinesterase (AChE) functions in the synaptic gap to break down ACh. Inhibition of AChE has been shown effective in improving memory loss, and all current drugs used in the treatment of Alzheimer's disease are AChE inhibitors.

Galanthamine (GAL; see chemical drawing, compound **1**) is a natural product found in *Galanthus nivalis* (common snowdrop, a type of lilly), which inhibits AChE. In addition, it shows some activity on the ACh receptor, which may provide additional modes of treatment.

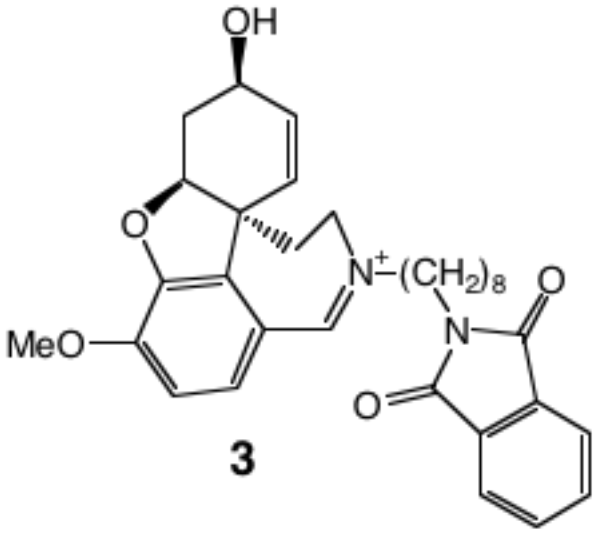
In an attempt to make more potent and specific compounds, several derivatives of GAL were prepared by the group of Claude Thal at the CNRS, Gif-sur-Yvette, outside of Paris. Three compounds were soaked into crystals of AChE, two of which (**3** and **5**) were collected at ESRF during this beam time. The results have been published in JACS, (Greenblatt *et al*., 2004, **126**, pp. 15405-15411).


OH
O
N–Me
MeO

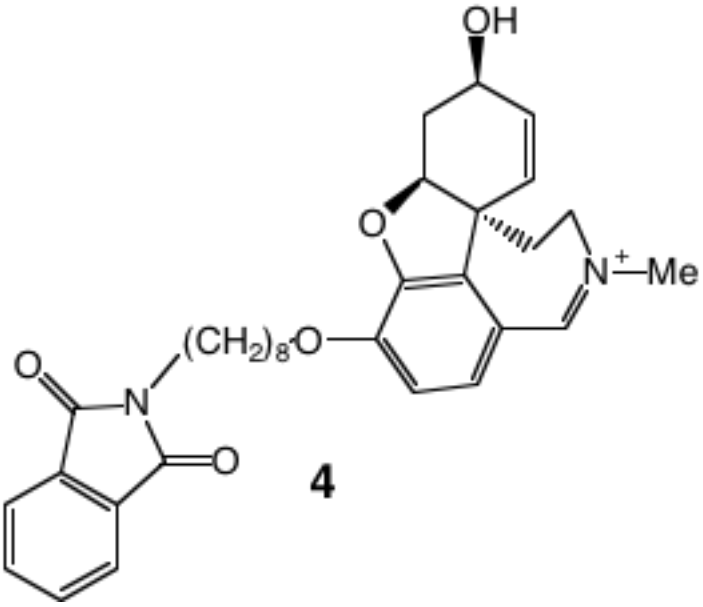
1


OH
O
N–(CH2)8
O
N
O
MeO

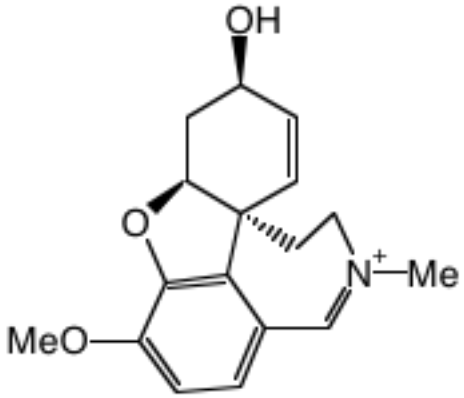
2


OH
O
N+–(CH2)8
O
N
O
MeO

3


OH
O
N+–Me
(CH2)8O
O
N
O

4


OH
O
N+–Me
MeO

5