



S344 Organic chemistry: a synthesis approach

Video Notes

Video 1 Birth of a drug

Pre-viewing notes

This video is concerned with the development of a new drug for the treatment of the medical condition known as hypertension. Hypertension, or high blood pressure, is thought to afflict something like 10-20% of the adult population in the UK, and is a major 'risk factor' for many forms of cardiovascular disease.

Blood pressure is the pressure exerted by the blood against the walls of the blood vessels. It is a consequence of the pumping action of the heart and of the diameter of the blood vessels, which affects the resistance to flow. It is highest in the arteries, which are connected most directly to the blood flow from the heart, and lower in the veins. Blood pressure changes from one minute to the next and is affected by a variety of factors such as age, state of health, physical activity, and response to external stimuli.

Hypertension is the result of constriction of the blood vessels which greatly increases the work of the heart, and can often lead to heart failure. In addition, resulting changes in the blood vessel walls, particularly the arteries, can lead to the formation of arterial plaque (a process known as atherosclerosis ('hardening of the arteries')) and an increased likelihood of thrombus (blood clot) formation. These effects cause a gradual blocking of the arteries, such that the circulation to the heart or brain can become so impaired that a heart attack or a stroke results.

Such undesirable consequences are to a great extent pre-ventable by effective drug treatment and to some extent by altering one's lifestyle. Unfortunately, the causes of hypertension are not well understood, though there are a number of risk factors such as excess weight, smoking, stress, excessive alcohol or sodium in the diet, and lack of exercise. Once hypertension is detected, in addition to eliminating as many risk factors as possible, it is advisable to resort to medication, which then has to be taken for the rest of the patient's lifetime.

But whereas patients willingly take a course of tablets or medicine three or four times a day for a week or two to combat an acute infection, there is much greater reluctance to complying with such treatment for many years. Clearly, a drug that only needed to be taken once a day would be likely to enjoy a significant advantage in terms of



convenience and hence effectiveness; for one thing, the patient is less likely to forget to take it.

How would you set about developing a drug for the treatment of a condition such as hypertension? And how could you design it such that its effects lasted for 24 hours so that it only needed to be taken once a day. This video relates the story of how just such a drug was developed by scientists at Pfizer, a pharmaceutical company with research laboratories at Sandwich, Kent and at Groton, Connecticut, in the USA. Appearing in the programme are two of the principal scientists involved, Dr Simon Campbell, Head of Discovery Chemistry, and Dr Michael Davey, then Head of Discovery Biology, and now Senior Director, Pfizer International.

The project arose from some research carried out in the 1960s at Pfizer's research laboratories in Groton, which led to the discovery of a new drug, prazosin, now widely used for the treatment of hypertension. After an initial follow-up programme, research in this area was discontinued until it was resumed later by scientists at Pfizer, UK. Why was the original programme discontinued? Why was it resumed? And what was the outcome?

You should now watch Video 1.