



A BETTER LIFE FOR ANGINA PATIENTS

Many thousands of middle-aged and elderly people are affected by attacks of angina. The symptoms are violent, sharp pain in the centre of the chest, often spreading to the neck or arms, brought on by exertion. The quality of life for people living in fear of such symptoms may be substantially improved by the constant protection afforded by Elgodipine, a new drug being developed by EUREKA project EU 425.

Elgodipine is being developed by Spanish and French scientists, who began trials in 1991 in Spain, France, the Netherlands, Germany and the United Kingdom. It works in basically the same way as some drugs used to control angina today, known as 'calcium antagonists', but could also offer some sig-

nificant advantages over these conventional treatments.

A kinder treatment for heart failure

Calcium antagonists work by blocking the inflow of calcium into muscle cells, which normally cause the artery walls to contract, thus decreasing the flow of blood to the heart. Blocking the calcium flow prevents the symptoms of angina, which are caused by the heart being starved of oxygen due to insufficient blood flow through the coronary arteries.

Elgodipine is a calcium antagonist, but has two important advantages over earlier drugs.

EUREKA



Chemical modifications of part of the drug molecule have greatly reduced any depressive effect on the heart muscle, suggesting that it may be possible to use the drug to treat cases of mild heart failure, as well as to protect against angina. Chemical changes also make Elgodipine stable in the presence of light. These two properties allow its use in 'angioplasties', a new technique for enlarging the diseased coronary arteries. This technique could substitute traditional by-pass surgery.

Elgodipine's stability also allows for it to be built into polymers now being developed for use in transdermal drug delivery systems, in which drugs seep slowly into the circulation through the skin at constant rates. This raises the hope that it will be possible to administer Elgodipine via an impregnated patch stuck to the skin, rather than orally or by infusion or injection. Tests are now underway to see if Elgodipine can be administered transdermally.

Ongoing Trials

The question that has to be answered before Elgodipine can be made available in a transdermal form is whether the drug will diffuse through the skin into the circulation at high enough levels to be effective. Studies involving several patients are now under way at St Bartholomew's hospital in London and the Queen's hospital in Belfast in Northern Ireland, to see if the dose delivery rate will be sufficient. If not, changes in formulation may solve the problem. Elgodipine is also currently being tested on twelve patients in the Netherlands as a treatment for mild heart failure, administered intravenously.

A Better Quality of Life

The development of Elgodipine began in Spain in the Instituto de Investigacion Y Desarrollo Quimica Bio (IQB) in Madrid. IQB is an eleven-year old company devoted to pharmaceutical research, with several products already undergoing trials for cardiovascular conditions. IQB are developing Elgodipine in partnership with Laboratories Delagrangé in Paris. The Delagrangé Group have marketed several therapeutic products all over the world.

The project leader, Dr Alvaro Galiano of IQB, says "EUREKA projects have such a good name that it has proved easy to interest cardiologists in trials of Elgodipine. Normally they are very hard to interest in a new drug without proven benefits. The European interest and international connections have enabled us to set up trials at several centres, with great advantages in speeding up progress."

Alvaro Galiano is very hopeful that the transdermal delivery route will prove feasible, because of the improvements this would bring to patients' quality of life. "Drugs taken orally create varying levels in the blood, with a risk of angina or heart attack at the lowest levels. Transdermal delivery would provide an absolutely constant rate of drug delivery, and so enable those at risk to feel secure and happy while undergoing moderate exertion." If all goes well, Elgodipine will be marketed by Delagrangé for angioplasty applications in 1993, and for angina applications in 1995.

Project Profile

EU 425	
Title:	Elgodipine Antianginal Calcium Antagonist
Announced at:	Vienna 1989
Participants:	<i>France</i> - Laboratories Delagrangé <i>Spain</i> - Instituto de Investigacion Y Desarrollo Quimico Biologico S.A. / Laboratories Delagrangé S.A.
Main Contact:	Mr Alvaro Galiano Instituto de Investigacion Y Desarrollo Quimica Bio (IQB) Madrid Tel: + 34 1 653 7043
Estimated Cost:	8.40 MECU
Time Scale:	4 years