

PHARMACEUTICALS FROM ANIMAL AND PLANT PRODUCTS

Natural products provide many fine chemical and biochemical extracts needed in the pharmaceutical, food and cosmetic industries. By-products from the meat industry are one rich source of such materials. This article gives some of the classes of material which can be extracted from meat industry by-products: steroids, polysaccharides, proteins, thymus extracts and hormones, and information on their end uses. Many of these are refined by New Zealand Pharmaceuticals Limited (NZP), which is also developing plant products including an Echinacea extract and an antioxidant extract.

INTRODUCTION

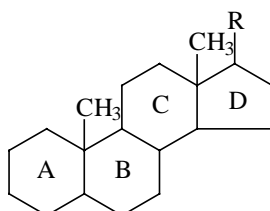
Animal parts which are by-products of the New Zealand meat industry are an excellent source of raw materials for making pharmaceuticals. In the early 1970s a group of NZ meat producing companies decided to extract and purify biochemicals from by-products of the industry. With Tasman Laboratories Ltd as the technical partner they formed New Zealand Pharmaceuticals Limited (NZP) to extract the biochemicals. NZP built a plant near Palmerston North and quickly became established as a successful manufacturer of bulk pharmaceutical raw materials. Initially the company only processed and made compounds from bile acids from the meat industry, but has now expanded to extract biochemicals from a range of natural raw materials and exports to more than 20 countries. From the beginning NZP has had a strong commitment to research and development, working with Massey University. This commitment is now enhanced by its growing association with the Crown Research Institutes and other Universities. It is now also actively engaged in research and development of plant products.

GLANDS AND TISSUES - PRODUCTS, SOURCES AND USES

Glands, organs of the body which excrete substances for metabolic use, are a major source of raw material. Glands or secretions used are the pancreas, pituitary gland, intestinal mucus, adrenals, bile and thymus. Other organs or tissues used include the spinal cord, the spleen and the trachea (windpipe).

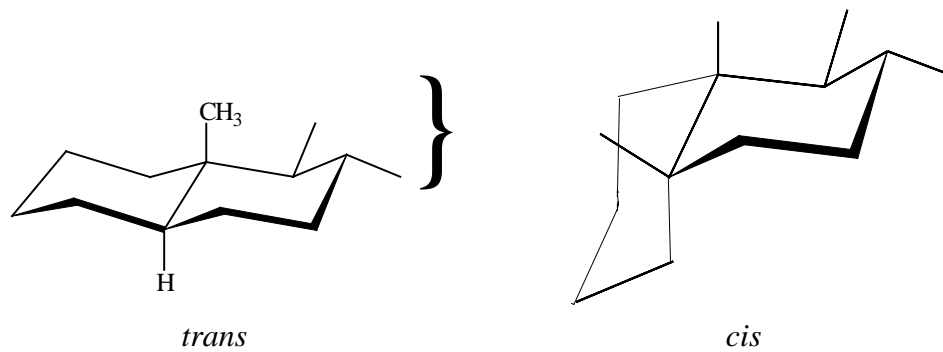
Steroids

Steroids are any compound based on the tetracyclic structure

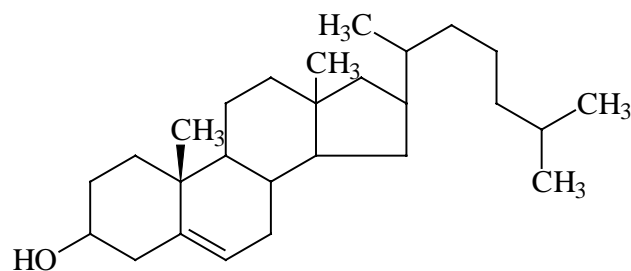


These compounds have multiple functions in biochemical systems acting as lipids (eg cholesterol), surfactants (the bile acids), hormones etc. Consequently they are found in various tissues. They are important pharmaceuticals as they may be used as extracted or as precursors for other drugs. An important chemical and biological difference in steroids is the stereochemistry of ring A with respect to ring B. If the methyl and hydrogen of the ring

junction are *trans* the molecule is more planar, whereas if they are *cis* the A and B rings are virtually at right angles as shown.



Cholesterol

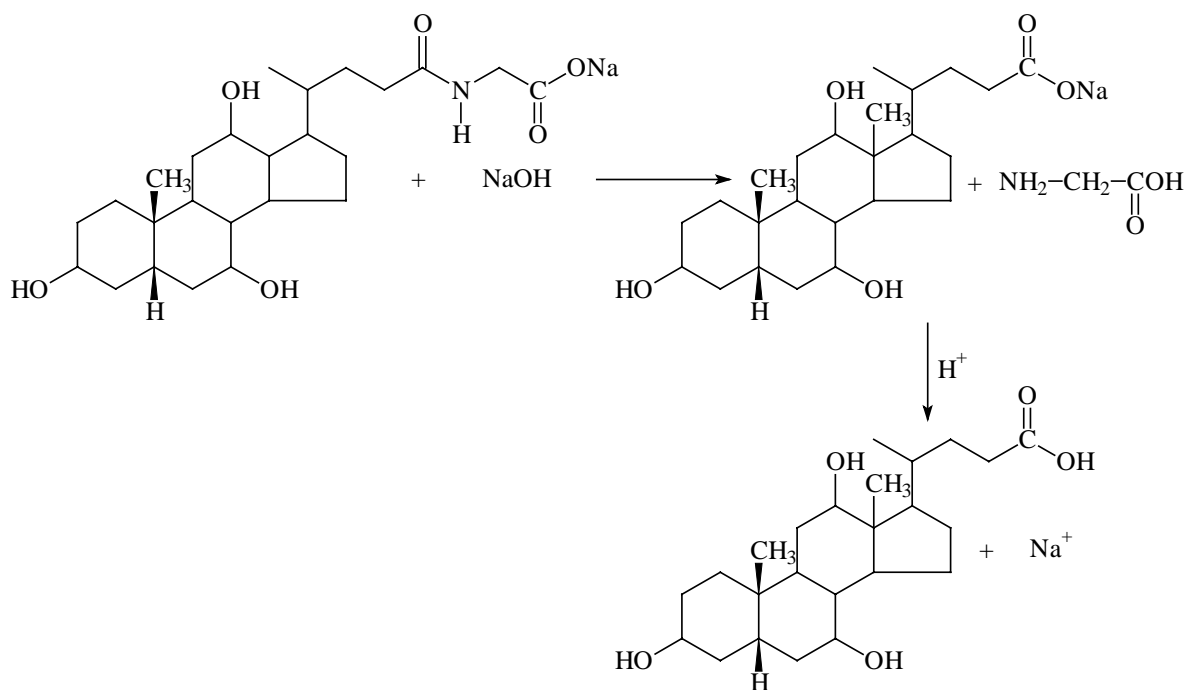


Cholesterol is a significant lipid in animal fats and the most abundant steroid. It can be extracted from the spinal cord of animals and used in production of vitamin D and sex hormones. This is not done in New Zealand. The double bond of the B ring makes the A and B rings nearly planar.

Cholic and deoxycholic acids

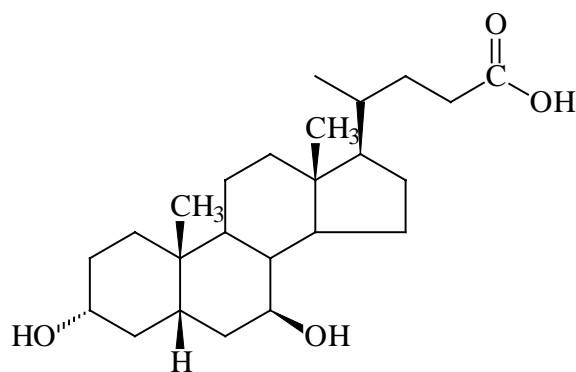
These two substances are the starting point for the synthesis of many steroids. NZP successfully produces free cholic and deoxycholic acids from bile using some relatively simple reactions involving alkali and acid. The reactions involved to make cholic acid from the bile acid/amino acid complex are given below.

In deoxycholic acid the hydroxy group on the B ring is replaced by hydrogen. They are used as starting materials for other steroidal compounds such as gallstone-dissolving drugs, hepatic drugs, digestive aids and corticosteroids. Sodium deoxycholate is used in biotechnology as a microbiological culture medium. Cholic acid is used as the starting material in a multi-step synthesis of ursodeoxycholic acid.



Ursodeoxycholic acid

Ursodeoxycholic acid is found naturally in bear bile. It is an Asian folk medicine used to protect the liver, but bears suffer terribly when people seek to extract the bile for medicinal use. Modern medical research has proved that ursodeoxycholic acid is an effective drug in the treatment of liver disease. Bears cannot be used as a source since large quantities of it are required as a pharmaceutical. Cholic acid is used as the starting material in a multi-step synthesis of ursodeoxycholic acid.

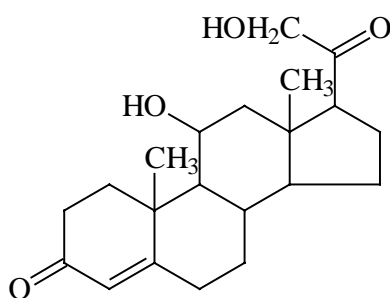


Ursodeoxycholic acid

Corticosteroids

Corticosteroids are a group of steroids that are used as anti-inflammatories to reduce swelling in the respiratory systems of asthma patients. One such steroid which is derived from bovine

adrenals is *corticosterone*, shown below. They are also extracted directly from the cortex of adrenal glands.



Corticosterone

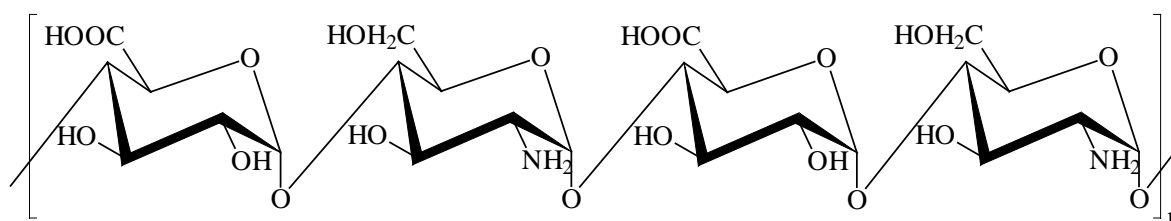
Other bile products

Bile powder is used as nutraceutical to aid digestion, and in aquaculture as a prawn feed ingredient. Mixed bile acids is also used in prawn feed and in poultry and pig foods also. Natural taurine, (an amino acid, not a steroid) is used in infant milk formula to make it more like human milk, in health tonics ("smart drinks"), and for the prevention of side effects from excess alcohol consumption.

Polysaccharides

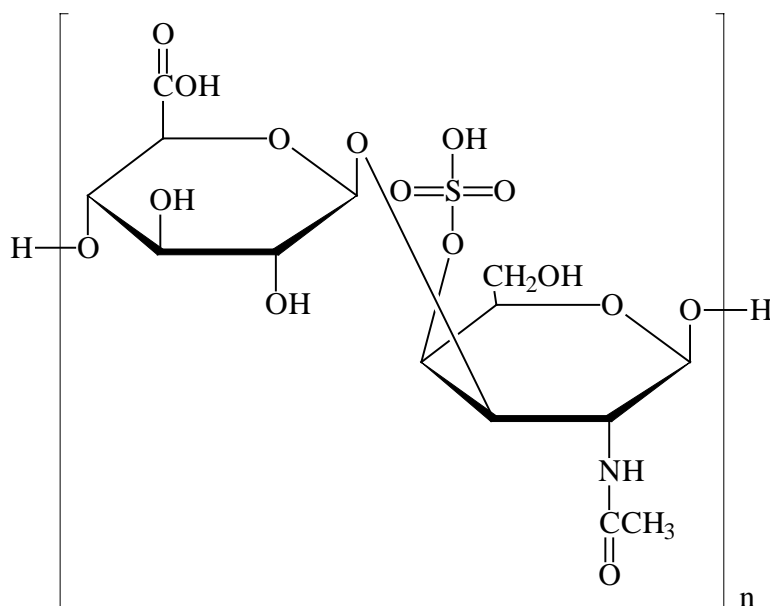
Glycosaminoglycans

These are aminopolysaccharides which are found in various forms throughout most animal tissues. Heparin has the basic structure shown below with some OH and NH₂ groups being sulfated and some NH₂ groups acetylated. It is obtained from intestinal mucosa mainly from sheep and pigs. Heparin is used commercially as a blood anticoagulant to prevent blood from clotting during operations or during blood dialysis. Derivatives of heparin and similar glycoaminoglycans are used to improve peripheral blood circulation. As a cosmetic heparin (applied topically) is used to reduce bruising and sometimes as a moisturiser.



Chondroitin sulfate

This polymer, a component of cartilage, is extracted from bovine trachea (windpipes). It is used as a nutraceutical in health food drinks and in a preparation for the preservation of eyesight; in cosmetics because of its moisturising properties and because it possibly increases elasticity and pliability of skin; and in veterinary use, where a derivative is injected into the joints of animals to relieve inflammation.

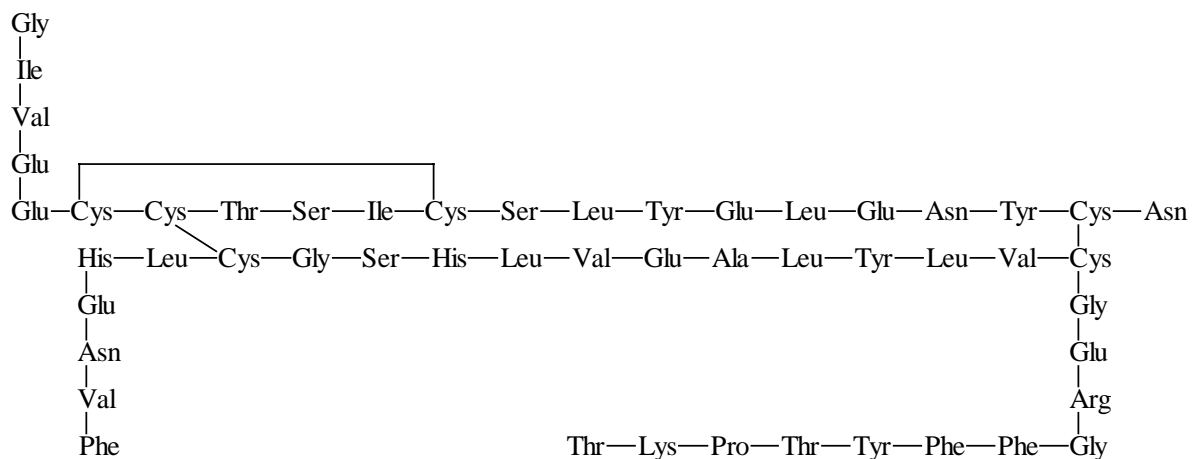


Chondroitin sulphate A

Proteins

Insulin

Insulin is a hormone consisting of two linked polypeptide chains (see below). It regulates blood sugar levels, and is missing in diabetic individuals. It is obtained from the pancreas. The structure given below is of human insulin, which is similar but not identical to the bovine and porcine insulin produced by the Meat Industry. It is not a NZP product.



Pancreatin

Pancreatin is a mixture of digestive enzymes consisting primarily of amyllopsin, trypsin and steapsin. It also comes from the pancreas and is used in pancreatitis control. NZP do not extract these.

Ferritin

Ferritin is an iron storage protein extracted from horse (equine) and cattle (bovine) spleens and used in the treatment of iron-deficiency anaemia.

Protein hydrolysis products

Hydrolysis of various proteins breaks them down into smaller polypeptide molecules. Peptones are obtained from enzyme catalysed hydrolysis and hydrolysates from acid catalysed hydrolysis. Meat peptone is used in biotechnology as a nutrient in vaccine production and in microbiological culture medium. Casein peptone (from milk) is also used as a culture medium while casein hydrolysates are used as an amino acid supplement (a nutraceutical) and in cosmetics. Collagen hydrolysate is obtained from the collagen of bovine trachea (windpipe) and is used in arthritis remedies (a nutraceutical) and in shampoos and skin creams (cosmetics).

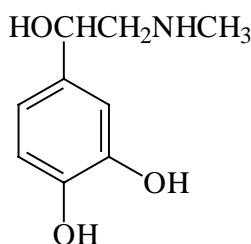
Thymus extracts

Thymus glands of neonatal calves are a source of products. Thymus peptides are used for the treatment of immuno-deficiency diseases. Thymopur NZ-25 (an NZP product) is used in cosmetics to possibly slow skin aging processes and in hair care products because of its film-forming properties and as a source of peptides and amino acids.

Hormones

Adrenalin

Adrenalin can be extracted from the inner portion of the adrenal glands. It is a trisubstituted benzene and is used as a heart stimulant.



Pituitary gland hormones

Hormones from this gland can be used for growth promotion and for lactation (milk production) induction.

Neither of these extracts are NZP products.

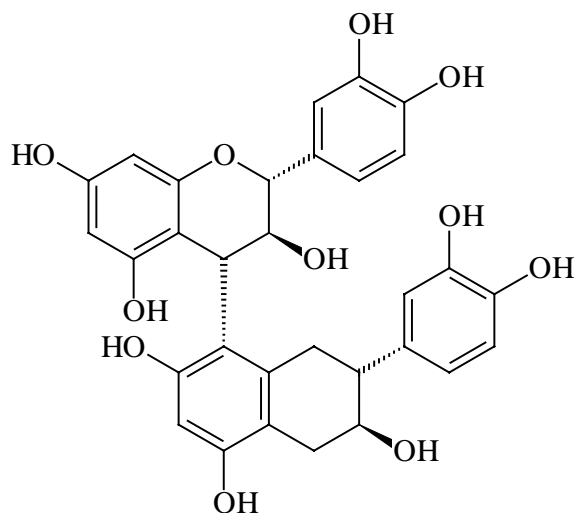
PLANT PRODUCTS

NZP is now expanding into this field for dietary supplements. Here just two areas are covered.

ProenOthera™

NZP have introduced a new name for a unique plant extract that is high in flavonoid content. Flavonoids have been shown to possess anti-oxidant properties and people in the medical and dietary supplement sectors suggest that an increase in dietary flavonoids and related compounds could be beneficial to our health. One popular argument in support of flavonoid anti-oxidants is based on the "French paradox". People living in France eat a very fatty diet but unlike those of us in English-speaking countries, the people in France do not suffer such a high mortality from heart disease. Possibly French people suffer less because red wine is a part of their regular diet and from wine they consume a high level of flavonoid anti-oxidants. This modern legend has increased the support for anti-oxidant dietary supplements based on

flavonoids and has increased the promotion of red wine! Procyanidin B3 is a representative flavonoid in ProenOthera™.

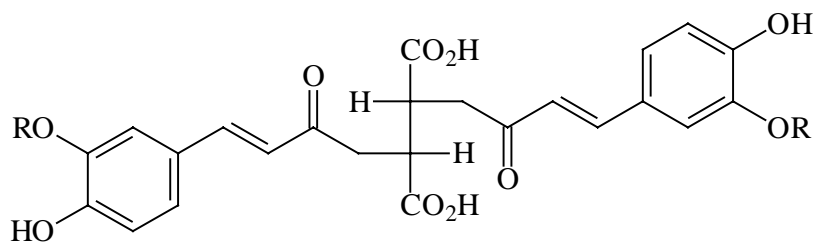


Procyanidin B3

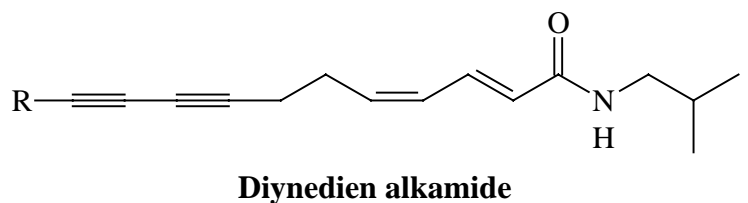
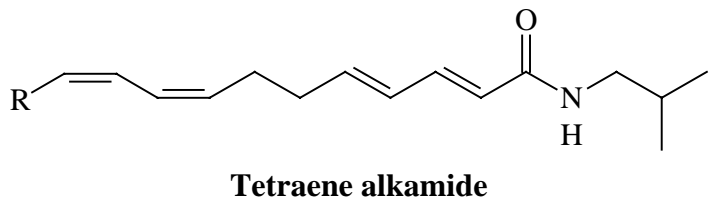
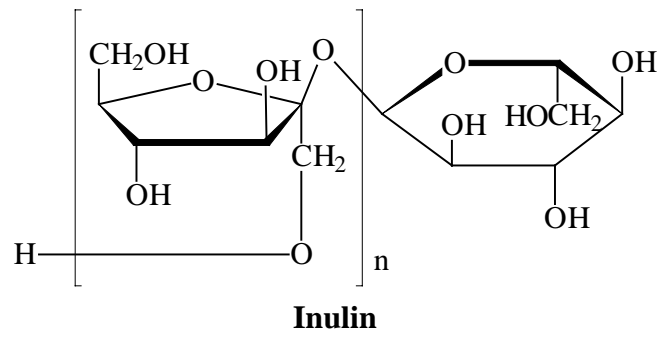
Products from Echinacea

The formulation of herbal medicines is based mainly on tradition and experience. Research over recent years has shown that many traditional herbal remedies have proven efficacy against diseases. Often, through a genuine misunderstanding of the low stability of the active factors, herbal medicines are sold which lack the original and claimed potency of the fresh plant. Another consideration, since the licensing of herbal remedies is not strictly controlled, is that some preparations are "doctored".

Echinacea is a flowering plant native to North America. The roots and tops of *E. angustifolia* and *E. purpurea* are traditionally used as immune-stimulants for the treatment of colds and influenzas (nutriceuticals). Scientists at NZP are working with analysts at the Crown Research Institute, Crop and Food Research, organic growers and retail companies to produce an Echinacea extract high in active compounds from a NZ organically grown echinacea. Echinacea contains three families of components thought to contain the biological activity, one antioxidant and two immune-stimulants. The antioxidants are polyphenolic compounds such as chicoric acid, and the factors thought to be immune-stimulants and anti-inflammatory are polyunsaturated fatty acid isobutyl amides and polysaccharides (including inulin and arabinogalactans). The true source of the biological activity is still under discussion but these classes of chemicals have all been cited to have the appropriate activity.



Chicoric acid



Written by John Packer and Selwyn Yorke (NZP) also incorporating material on the meat industry supplied by R.C. Rendle.