PhytoChol®

Vegetal-derived, Semi-synthetic

Cholesterol

Cholesterol has numerous pharmaceutical applications including drug delivery [lipid liposomes, etc.] and cell cultures. Cholesterol is also commonly used in cosmetics.

Naturally occurring cholesterol is found almost exclusively in animals with the highest concentrations being in the brain, spinal cord and fats and oils. There are currently two main commercial routes to obtain cholesterol: extracting it from the spinal cords of cattle, and from lanolin, the natural grease found on wool. Today, commercial quantities of natural cholesterol are routinely available in 95 per cent purity, and can be further processed to an assay of >98 per cent.

With increasing frequency, regulatory authorities are cautioning that natural (i.e. animal-based) cholesterol could pose health hazards to humans. This warning has created a serious headache for cosmetic formulators and pharmaceutical manufacturers alike. Concern about transmitting animal-based diseases to humans -- *bovine spongiform encephalopathy* (BSE) being the best-known example -- has made pharmaceutical and cosmetic companies think twice about using animal-derived raw-materials like cholesterol in their products.

Many regulatory agencies, including the US Food and Drug Administration (FDA), now require stringent proof that animal material used in drug and cosmetic preparation is safeguarded against the risk of transmission to humans. This requires careful monitoring of animals from which the cholesterol is sourced and tracking the product from the farm to the slaughterhouse or shearing shed, and then onward to the fine chemical manufacturer who extracts and purifies the Cholesterol for use.

Until recently, sourcing Cholesterol from animals in countries where there are currently no reported cases of BSE was considered a solution to this problem. However, the recent occurrence of BSE in Japan, Canada and the US suggests that geographic isolation is no longer an adequate safety barrier. Given the ubiquitous availability of Cholesterol on the world market, the only certain way of eliminating the risk is to find a non-animal replacement for this versatile animal product.

The possibility that cosmetics or pharmaceuticals may be contaminated by harmful viral or protein adulteration from animal-based cholesterol is not a risk that is unique to only cholesterol-based products, but rather one common to all products processed from animal or human material. Institution of steps aimed at regulating raw material sourcing, quality control and design and

control of the manufacturing process can minimize these risks. But to eliminate the risks completely, regulatory authorities recommend using either synthetic or plant-derived material wherever possible.

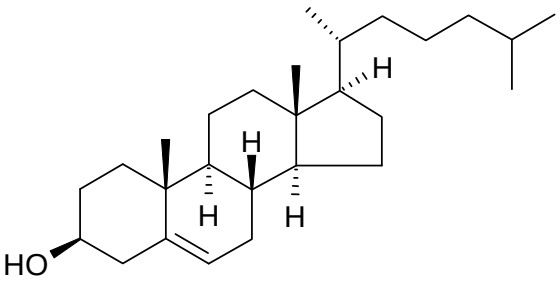
To this end, at least one fine chemical manufacture now offers a plant-derived, semi-synthetic cholesterol. However, at $34,500/Kg, the price of this material makes it impractical for all but the highest value-added applications.

At the same time, some suppliers have begun the misleading practice of marketing what they describe as enzymatically-derived cholesterol -- the implication being that such Cholesterol is the product of an *in vivo* microbiological synthesis. What these suppliers fail to state is that the principal raw material for such processes is the residuals (tailings) left from the processing of ***animal*** fats -- a substantial fraction of which consists of free cholesterol and cholesterol esters [cf. US 3,919,045]. Following treatment with esterase, the resulting Cholesterol is obtained by solvent extraction of the emulsified medium. Cholesterol derived in this manner, of course, is not a bio-synthetic material at all, but rather an animal-based product that is no more or less free of potentially harmful viral or protein adulteration than any other source of animal-derived cholesterol.

One means of avoiding the problems associated with using animal-based Cholesterol would be to obtain it from plant sources. Unfortunately, Cholesterol is the only sterol not found to any significant degree inn plants. It follows, therefore, that plant-derived cholesterol must necessarily be, at the minimum, semi-synthetic.

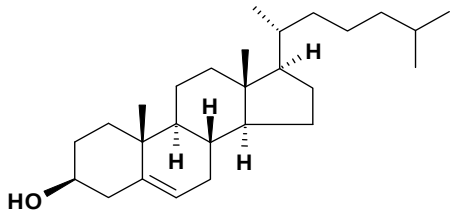
Relying on the fact that various readily available plant sterols possess the requisite critical A, B, C, and D ring structure of cholesterol, Wilshire Technologies has developed a commercially viable, practical route to plant-derived (vegetal), semi-synthetic Cholesterol (**PhytoChol®**) that is chemically and physically indistinguishable from the animal-based product.

Plant Sterol ⟶



Cholesterol
(PhytoChol®)

Certificate of Analysis

Product Name	**PhytoChol®**
syn:	Cholesterol; 3β-Cholest-5-en-3-ol (vegetal-derived, semi-synthetic)
Structure	
CAS No.	**57-88-5**
Mol. Formula	**$C_{27}H_{46}O$**
Mol. Weight	**386.66**
Source	**Plant-derived**

Test	*Specification*
Appearance	**White Crystals**
Identity	**USP, EP; IR, NMR**
Mp	**149-150 ^{0}C**
Assay	
Cholesterol (EP, USP)	**≥ 99%**
Total Impurities	**< 200 ppm**
Sp. Rot., $[\alpha]_D^{25}$	**< - 39 ^{0} (*c* = 2.0, $CHCl_3$)**
Heavy metals (As, Pb)	**< 10 ppm**
LOD	**< 0.15 %**
Sulfated Ash	**< 0.1 %**
Acidity	**EP, USP**
Solubility	**EP, USP**

Wilshire Technologies, Inc. ***Princeton, NJ 08542*** ***T: + 1.609.683.1117***