β-Sitosterol

A Plant-based Cholesterol Substitute

Cholesterol has numerous pharmaceutical applications including drug delivery [lipid liposomes, etc.] and cell cultures. Cholesterol is also a common ingredient in many cosmetics.

Naturally occurring cholesterol is found 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.

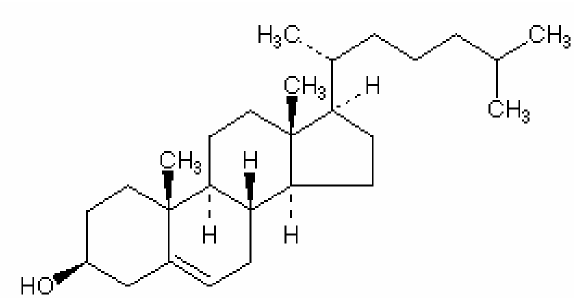
Until recently, sourcing Cholesterol from animals in countries where there are currently no reported cases of BSE was considered a solution to this problem. However, the recent occurrence of BSE in Japan suggests that geographic isolation is no longer an adequate safety barrier. Given the ubiquitous 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.

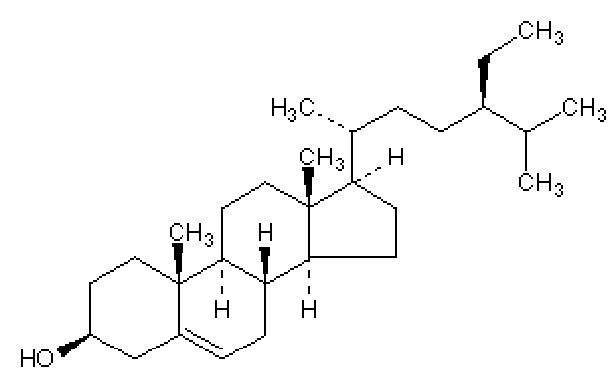
To this end, at least one fine chemical manufacture now offers a plant-derived, semi-synthetic cholesterol. However, at \$20,000-\$30,000/Kg, the price of this material makes it impractical for all but the most value-added applications.

A much less costly alternative would be the use of a totally plant-based Cholesterol substitute. One such compound is the plant sterol **β-Sitosterol**. There are several reasons for giving such a proposal careful consideration. First, as Figure 1 shows, there are striking similarities in the structural nature of these two sterols. Thus, the A, B, C, and D ring of cholesterol and **β-Sitosterol** are identical. Indeed, the only structural difference that exists between these two compounds is the presence of an additional ethyl group in the 24β position of **β-Sitosterol** that is not present in Cholesterol.

Figure 1.



Cholesterol



β-Sitosterol

Second, these very similar analogues share close physical properties:

	Cholesterol	***β-Sitosterol***
Mp	148 ^{0}C	140 ^{0}C
[α]$_D$ (*c* = 2, $CHCl_3$)	-39.5^0 (@ 25 ^{0}C)	-37^0 (@ 25 ^{0}C)

Third, their close physical properties are paralleled by the virtually identical chemical properties. Thus, any transformation performed on cholesterol is equally applicable to **β-Sitosterol**.

Fourth, the medical qualities of both sterol have been studied extensively and β-Sitosterol has documented theraputic activity[1-3] as, *inter alia*, an anticholesteremic.

References

(1) Studies on inhibition of cholesterol absorption S. M. Grundy, H. Y. I. Mok, *ibid.* pp 112-118; I. Ikeda, M. Sugano, Biochim. Biophys. Acta 732, 651 (1983).

Cont'd

(2) Inhibition of induced carcinogenesis: N. D. Nigro et al., *J. Natl. Cancer Inst.*, ***69***, 103 (1982).

(3) Clinical trial in treatment of prostatic adenoma: H.-P. Szutrely, *Med. Klin.* ***77***, 520 (1982); book "Monographs on Athero sclerosis," Vol. 10, T. B. Clarkson, *et al.*, Eds., entitled "Sitosterol" by O. J. Pollak, D. Kritchevsky (Karger, Basel, 1981) pp. 219.

Product Specifications

Name	**β-Sitosterol**
Syn.	24β-Ethylcholesterol; 22:23-Dihydrostigmasterol; α-Dihydrofucosterol; Δ^5-Stigmasten-3β-ol; α-Phytosterol
CAS No.	**83-46-5**
Mol. Formula	$C_{29}H_{50}O$
Mol. Weight	414.7

Test	*Specification*
Appearance	White solid
Mp	139-141 ^{0}C
Assay (glpc)	$\geq$ 70%; $\geq$95%
Specific Rotation, $[\alpha]^{25}_D$	-36^0 -37^0 (c = 2, $CHCl_3$)
LOD	<0.5%
Heavy Metal (Pb, As)	<20 ppm

NOTE: *Like Cholesteryl esters, many esters of β-Sitosterol have valued qualities as liquid crystals.* ***Wilshire*** *offers a broad selection of β-Sitosteryl esters suitable for such applications including, but not limited to, β-Sitosteryl Benzoate, Butyrate, Cinnamate, Acetate, Nonanoate, Octanoate, Oleate, Phenylacetate, as well as β-Sitosteryl Chloroformate. Contact us with your request.*