Niemann-Pick type C, or NPC for short, is an early-onset childhood disease, which has been diagnosed in about 200 people in the U.S. NPC, exhibits progressive neurological degeneration, associated with hepatomegaly and splenomegaly. The disease, at the cellular level, is a result of improper trafficking of lipids such as cholesterol and glycosphingolipids (GSLs) to lysosome-like storage organelles (LSOs), which become engorged with these lipids. It is believed that the initial defect in trafficking, whether of cholesterol or a GSL, results in an eventual traffic jam in these LSOs. This leads to the retention of not only other lipids, but also of transmembrane proteins that transiently associate with the late endosomes (LE) in normal cells, on
their way to other cellular destinations such as the trans-Golgi network (TGN) (Mukherjee et al., 2004).

A silent mutation of Niemann-Pick C1-Like 1 (NPC1L1) and apolipoprotein E4 modulates cholesterol absorption in primary hyperlipidemias a study reveals (Lupattelli et al., 2013).

Embryonic Bilberry extracts contain considerable amounts of Fucosterol and Isofucosterol, which are selective liver X receptor modulators that regulate the expression of key genes in cholesterol homeostasis in macrophages, hepatocytes, and intestinal cells. Fucosterol is a dual-LXR agonist that regulates the expression of key genes in cholesterol homeostasis in multiple cell lines without inducing hepatic triglyceride accumulation. Moreover, it induced the transcriptional activation of ATP-binding cassette transporter (ABCA1), ATP-binding cassette sub-family G member 1 (ABCG1), and Apolipoprotein E (ApoE), key genes in reverse cholesterol transport, and thereby significantly increased the efflux of cholesterol. Fucosterol also regulated intestinal Niemann-Pick C1-Like 1 (NPC1L1) a critical mediator of cholesterol absorption and ABCA1 in Caco-2 cells (Hoang et al., 2012).

Dysregulation of cholesterol homeostasis in the brain is increasingly being linked to chronic neurodegenerative disorders, including Alzheimer’s disease (AD), Huntington’s disease (HD), Parkinson’s disease (PD), Niemann-Pick type C (NPC) disease and Smith-Lemli Opitz syndrome (SLOS), (Vance, 2012).

They are a total of 42 phytochemicals found in Bilberry embryonic plant extracts that are responsible for cholesterol homeostasis.

Below is a breakdown of all the references from my upcoming MEP™ Encyclopedia in support of embryonic Bilberry plant extracts for cholesterol homeostasis.

A study demonstrated that anthocyanins are capable of more bile acid bindings lowering cholesterol levels in humans (Hinkle, 2013). Bilberry young shoots and embryonic fruits contains a total of 23 anthocyanins (Choi et al., 2010; Kim et al., 2012; Müller et al., 2012). Anthocyanins have higher antioxidant properties and higher influence on cholesterol concentration in erythrocyte’s membranes than simple hydroxycinnamic acids (Fimognari et al., 2005).

Asperuloside (a monoterpenoid iridoid glucoside): a study after four weeks, demonstrated that body weight and white adipose tissue weight, plasma triglyceride levels and total cholesterol levels were significantly inhibited by the 30% MeOH fraction, which contain much higher levels of asperuloside than any other fractions. Chronic administration of asperuloside containing plant suppressed increases in model mouse body weight, white adipose tissue weight, plasma triglyceride levels and free fatty acids (FFAs) levels. These results suggest that asperuloside has important anti-obesity activity and hypocholesterolemic effects (Hirata et al., 2011).

B-Sitosterol is a minor hypocholesterolemic agent. Cycloartenol synergistically potentiates the hypocholesterolemic effect of β-sitosterol (Sugano et al., 1997). Campesterol, is known to have a cholesterol-lowering effect. Structure-specific effects of individual phytosterol constituents have recently shown that saturated phytosterols called phytostanols are more efficient compared to unsaturated compound's phytosterols in reducing cholesterol levels (Ling et al., 1995). Furthermore, it was demonstrated that sitostanol only causes cholesterol malabsorption, without interfering with the absorption of important fat-soluble vitamins (Howard et al., 1997).
(+) - catechin and (−) - catechin are well-known histidine decarboxylase (HDC) inhibitors, and hypocholesterolemic agents (Duke, 1992). (−)-Epicatechin hypocholesterolemic agent (Duke, 1992).

Chlorogenic acid (CGA) modifies plasma and liver concentrations of cholesterol by 44% and triglycerides by 58% and in the liver triglyceride concentrations by 24%. Significant differences (p < 0.05) in the plasma, liver, and spleen concentration of selected minerals were found in chlorogenic acid-treated rats. In vivo, CGA was found to improve glucose tolerance, decreased some plasma and liver lipids, and improved mineral pool distribution under the conditions of this study (Rodriguez et al., 2013).

Another study demonstrated that ferulic acid (FA) had relatively similar hypolipidemic actions and could be effective in lowering the risk of high-fat diet-induced obesity (Jin et al., 2010).

Isoquercitrin significantly decreased plasma C-peptide, triglyceride, and total cholesterol and blood urea nitrogen levels after 35 days (Zhang et al., 2011).

Oleanolic acid (OA), an extract rich in OA derivatives, caused rapid alterations in cholesterol homeostasis, presumably by depleting cholesterol in lipid rafts (LRs), which subsequently interfered with signaling mediated by LRs. They also showed that BN107 or OA treatment in ER- breast cancer cells resulted in rapid and specific inhibition of LR-mediated survival signaling, namely mTORC1 and mTORC2 activities, by decreasing the levels of the mTOR/FRAP1, RAPTOR and RICTOR. This is the first report demonstrating possible concomitant inhibition of both mTORC1 and mTORC2 activities by modulating the levels of protein constituents present in these signaling complexes, and thus provides a basis for future development of OA-based mTOR inhibitors (Chu et al., 2010).

Ortho-Coumaric acid is beneficial for the suppression of high-fat-diet-induced dyslipidemia, hepatic steatosis, and decreasing oxidative stress thereby reducing obesity. It enhances the levels of glutathione (GSH), peroxidase (GPx), GSH reductase (GRd), and GSH S-transferase (GST) in liver tissue assisting in the detoxification process. It reduces elevated serum levels of cholesterol, triglycerides, insulinemic, and reduced leptin (Hsu et al., 2009).

Pectin A, a demulcent, hemostatic, reduced the absorption of cholesterol from bile or food (Ginter et al., 1979; Mietinnen et al., 1977).

Polysaccharides reduce cholesterol levels (Cheng et al., 2011).

Resveratrol is a stilbene hypocholesterolemic agent (Duke, 1992).

A study demonstrated that polyunsaturated fatty acids in Caco-2 cells and sterols in HepG2 cells significantly reduced the messenger RNA expression levels of Niemann-Pick C1-like 1 (NPC1L1), scavenger receptor class B type 1, low-density lipoprotein receptor (LDLR), and 3-hydroxy-3-methylglutaryl-coenzyme A reductase. Importantly, sitosterol and stigmasterol reduced the messenger RNA levels of genes to a similar extent as cholesterol. This data supports the hypothesis that unsaturated fatty acids and phytosterols can act as signaling molecules and alter the expression of genes involved in cholesterol transport and metabolism (Park et al., 2013).

Ursolic acid lowers cholesterol through the activation of peroxisome proliferator-activated receptor (PPAR)-α (Jia et al., 2011).
Vitamin C Complex also reduces cholesterol (Ginter et al., 1977). Another study with vitamin C, given for a minimum of 4 weeks, can result in a significant decrease in serum LDL cholesterol and triglyceride concentrations (McRae, 2008).

Xyloglucans; a study concluded that xyloglucan plasma lipids, total lipid, cholesterol, triglyceride and β-lipoprotein were each reduced 14–17% by hydrolyzed xyloglucan (Yamatoya et al., 1996).

Embryonic Bilberry plant extracts in injectable form thru parenteral delivery route should be considered for a clinical trial study in the treatment of NPC disorder. There would not be the side effects of deafness, which are now being reported from the present study treatment associated with cyclodextrin drug. A wide variety of effective biological drugs already exist in nature. They would, in fact, be the answer to many of our health problems if not for mans greed and the inability to patent an existing known plant for the medical treatment.

Now add to your prescription Olive and Rosemary and you have a hefty support for cholesterol and triglyceride homeostasis with no side effects like that of synthetic statins.

**PROTOCOL FOR CHOLESTEROL HOMEOSTASIS**

**Bilberry** – Vaccinium Myrtillus (young shoots of leaves and embryonic fruits) 1:20, 15 gtt, tid, QD.

**Olive** – Olea Europaea (young shoots) 1:20 15-25 gtt, tid, QD. Beware that high dose of Olive 25 gtt, tid, QD is contraindicated in hypothyroidism which will further reduce the level of T-3 but at a dose of 15 gtt, tid, does not cause any such side effect. If this is observed it is easily reversible upon discontinuation with no longer consequences. The reason being is that often in chronic fatigue syndrome (CFS) you will need in acute viral reactivation high dose of Olive to rid the patient of severe asthenia and this is only achieved by a dose of 25 gtt, tid, QD and often CFS patients suffers also of hypothyroidism or adrenal dysfunction. You can easily remedy this with the concomitant use of Oak – Quercus Pedonculata / Robur (buds) or White Birch – Betula Pubescens (flower male-catkins) at a dose for both 10-15 gtt, tid, QD.

**Rosemary** – Rosmarinus Officinalis (young shoots) 1:20, 15 gtt, tid, QD. Mandatory to assist the liver in the processing of all fats-lipids.

In the defective fatty acid's metabolism and/or fatty acids oxidation causative of inflammation. You now can permanently correct these conditions with the help of two very unusual unsaturated fatty acids. Both are polyunsaturated fatty acids (PUFAs) (1) Delta5-unsaturated polyethylene-interrupted fatty acid (delta5-UPIFA), also known as juniperonic acid (20:4 Delta-5,11,14,17) and (2) Sciadonic acid (20:4 Delta5-all-cis-5,11,14) that guarantees the conversion of unsuitable fatty acids into essential fatty acids (EFA) especially into eicosapentaenoic acid (EPA), (Tanaka et al., 2001). Without the need for costly supplemental fish oils that are highly prone to oxidation to lipid peroxides and other secondary oxidation products (Albert et al., 2013), in addition to often being tainted with arsenic and ultimately never corrects the problem (LeBlanc et al., 1973).

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<th>MEP Source</th>
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<td><strong>Juniperonic acid</strong></td>
<td>20:4 Delta-5,11,14,17</td>
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<td><strong>Sciadonic acid</strong></td>
<td>20:4 Delta5-all-cis-5,11,14</td>
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<td>Mountain Pine – Pinus Montana (buds)</td>
<td>31% P</td>
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<tr>
<td>Silver Fir – Abies Pectinata (young shoots)</td>
<td>19% P</td>
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<tr>
<td>Juniper – Juniperus Communis (young shoots)</td>
<td>10.1% P</td>
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<td>Cedar of Lebanon – Cedrus Libani (young shoots)</td>
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<tr>
<th>Mountain Pine – Pinus Montana (buds)</th>
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<td>Silver Fir – Abies Pectinata (young shoots)</td>
<td>4.0%</td>
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<td>Cedar of Lebanon – Cedrus Libani (young shoots)</td>
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The most effective embryonic herb is **Mountain Pine – Pinus Montana (buds)** which can be given at a dose of 15-30 gtts, tid, QD. This plant is also a hypolipidemic agent in addition to correcting defective fatty acid's metabolism this will take anywhere from six months to one year to accomplish but at least not like that of fish oil chronic need of supplementation. Mountain Pine is a natural profen and the *polycrest* for stimulating our own production of glucosamine and chondroitin in the body.

Silver Fir – Abies Pectinata (young shoots): do not exceed 5-20 gtts, tid, QD. More for extreme in age infancy with growth problems or geriatric with advanced osteoporosis.

In teenagers, young adults until the age of 55 it would be more appropriate to used Horsetail – Equisetum Arvense (young shoots) which is nature methylsulfonylmethane (MSM) and when afflicted with osteopenia or accomplish osteoporosis. At a dose of only 10 gtts, tid, QD for six months to one year is almost guaranteed to reverse bone density back to normal. I have never witness anyone single plant alone this effective for this condition. Furthermore, excellent for phenolsulfotransferases (PSTs) deficiency.

Juniper – Juniperus Communis (young shoots) 10.1% P is chosen when you have both renal dysfunction and renal failure with defective fatty acid's metabolism.

There is no need for supplemental toxic fish oils tainted with high levels of arsenic or where once ingested 50% of it now known to oxidize in the human body.

Marine oils are a thing of the past and are no longer recommended. They are derived from toxic; fish, krill, shellfish, calamari, or algae (most of them toxic) and vastly differ from terrestrial plant sources of omega-3 fatty acids such as hempseed (favorite with over 25,000 different uses) or flaxseed (high in lignans – phytoestrogen) as they contain the long-chain polyunsaturated fatty acids (LC-PUFAs), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). Terrestrial plant sources of omega-3 fatty acids show promise, particularly in the prevention of cardiovascular disease (CVD), the treatment of inflammatory disease improving early life neurodevelopment, preventing cognitive decline, and potential benefits to metabolism (Albert et al., 2013).

Phenolsulfotransferases (PSTs) deficiency or sulfoconjugation defects for the detoxification of xenobiotics and endogenous compounds (Yeh et al., 2004). In PST deficiencies, estrogen dominance is already present that is express with elevated lipids in the blood, especially total cholesterol. High stress alone can cause elevated cholesterol levels. Pseudo clinical PST deficiency is also common in inflammatory bowel diseases (IBD), Crohn’s disease, ulcerative colitis (UC), and peptic ulcers. All types of IBD have a mucosal layer turnover rate several times greater than normal. Symptoms of PST Deficiency for which Beech, Bilberry, Horsetail (MSM) and Rosemary are *polycrests* include: aggressive behavior, anger, autistic behavior, chronic fatigue (CFS) in adults, dark circles under eyes, diarrhea, excessive thirst, headache, head-banging, hyperactivity, IBD, inappropriate laughter, insomnia,
lethargy, losses of verbal, nonverbal, and lack of social abilities, night sweats, odorous bed clothing, red ears, red face self-injury behavior, and tiredness.

Please Note: when you use this protocol for elevated lipids levels and that on repeated laboratory monitoring and not appreciably reduce this is a clear sign of estrogen dominance check blood levels for estrone and estradiol and if menstruating can only be performed during the luteal phase for accuracy on a 28-day cycle this means between 18 and 21st-day from day one of the menstruating cycles is best. If either two estrogen is elevated, then to this protocol you would need to add an aromatase inhibitor, please refer to my article “In search of aromatase inhibitors.”

Lilac – Syringa Vulgaris (buds) is mandatory in coronary artery diseases like that of arteriosclerosis at a dose of 5-25 gtt, tid, QD dose dependent is based on the amount of plaque and level of hypertension. Lilac is the polycrest chelator of the arteries repeated Doppler sonography has shown after six months of continuous supplementation to reduce plaque by 40% on average and can be continued long term. Blood pressure monitoring is another determination factor for Lilac extracts higher doses lowering hypertension.

In males with low testosterone levels is often a sign of estrogen dominance converting testosterone to estrogen and can also be a sign of low progesterone for which Chaste Tree – Vitex Agnus Castus (young shoots) is the polycrest not to supplement progesterone but to assist in the body own production of progesterone. The dose can vary with Chaste tree in post-menopausal women Chaste tree is easier to evaluate based on the reduction of hot flashes. Whereas in the male population only your blood lab hormonal levels are the only way to monitor if you are dosing sufficiently. This should be monitored every 10 to 12 weeks from initiation. Chaste tree can be given 10-25 gtt, tid QD. Oriental Plane Tree – Platanus Orientalis (buds) 1:10 a total of 5 kaempferols in large amounts. This is the polycrest for aromatase inhibition dosage is 10-15 gtt tid, QD.

Lemon Tree – Citrus Limonum (bark) is polycrest for reducing the level of elevated C-reactive protein (CRP) and for the treatment of acid blood pH a sign of inflammation within the cardiovascular system the dose is 10-15 gtt, tid, QD and extremely reliable better than any Serrapeptase or Nattokinase enzymes courtesy of nature.

To increase the levels of low density lipoprotein (HDL) and for reducing elevated triglycerides the polycrest is Hazel – Corylus Avellana (buds) at a dose of 10-15 gtt, tid, QD. Beware that both Hazel and Lemon tree are anticoagulants and are not biphasic.

The polycrest for elevated fibrinogen are best reduced by Crab Apple – Malus Sylvestris (buds) 1:10 double strength 15-25 gtt, tid, QD.

They are other plants in MEP that can also play a major role in cholesterol homeostasis this protocol can be varied depending on everyone unique chemical profile some will require many anthocyanins for vasorelaxation and vascular integrity. Only by keep on studying your phytochemistry can you become more proficient in the design of custom-made Biotherapeutic programs addressing all in need for homeostasis.

30 References:


Howard V Barbara, PhD; David Kritchkevsky, PhD. Phytochemicals and Cardiovascular Disease. Circulation. 1997; 95: 2591-2593 DOI: 10.1161/01.CIR.95.11.2591.


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