

## Nutraceuticals as new therapeutic strategies for health and wellbeing

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Many innovative therapies are currently the focus of scientific research with a growing interest among both physicians and patients. There is an increased tendency to use nutraceuticals and/or biologic medical products in the treatment of common diseases, as well as more complex conditions that are more challenging to treat. In this context, a current goal of pharmaceutical research is to manufacture safer drugs with fewer adverse effects that more closely resemble the traditional "grandmother's" remedies that have been passed down through generations. Even in ancient Greece, Hippocrates wrote that even poison could be made suitable for curing pathology rather than causing morbidity and death. Closer to Hippocrates' vision, and very similar to his thinking, are Veronesi's statements for anti-tumor therapy (1), the new frontiers of pharmaceutical research for the composition of drugs against HIV infection (2) and Polio (3). Above all, to our great interest, is the intent of some pharmaceutical companies use nutraceuticals

to treat dyslipidemia, type 2 diabetes, as well as other diseases related to eating disorders. For instance, Curcuma longa, Silybum marianum, licorice (*Glycyrrhiza glabra*) and other similar aliments that have traditionally been used as nutritional supplements to improve the taste of foods or to reduce stress now are being used in the treatment of the metabolic syndrome (4-10). Recently, Curcumin, a component of traditional turmeric, Curcuma longa, based on its effect on lipid metabolism in the liver, has been suggested as therapeutic for hepatic steatosis (9). Silibinin modulates lipid homeostasis in hepatocytes, but also has a protective, antioxidative effect (4). Further, Oleocanthal, a phenolic compound, present in some varieties of olive oil, has anti-inflammatory effects comparable to those of Ketoprofen, a member of the propionic acid class of nonsteroidal anti-inflammatory drugs (11-14), while Chitosan, Ginseng, Berberine, Guggulsterone are commonly used for the treatment of dyslipidemia (7-9). Recently we showed that chitosan, derived

from fungal mycelium, reduce total (8%) and low-density lipoprotein (LDL) cholesterol (2%), triglycerides (16%) and increased high-density lipoprotein cholesterol (14%), with beneficial effect on lipoprotein subclasses as well, through reducing small, dense LDL (15). In addition, many studies have reported that Berberine lowers both elevated lipids and glucose, with beneficial effects on the cardiovascular system, and thus might be used in the treatment of the metabolic syndrome (16). Guggulsterone, a plant steroid of *Commiphora mukul*, decreases total and LDL cholesterol, representing a novel hypolipidemic and hypocholesterolemic agent (7,8). On the other hand, there are many medications and laboratory products which mimic the effect of certain enzymes or hormones (such as incretin hormones) naturally present in our body, but deficient in the case of some disease states. Such medications are the current favorites in medical practice (17). More precisely, some drugs are used as hypoglycaemic therapy by enhancing activation of the hormone glucagon-like peptide-1 (GLP-1) from the gastrointestinal tract. GLP-1 receptor agonists (e.g. Liraglutide) mimic the effect of endogenous GLP-1 while another class of medications suppress the activity of the enzyme dipeptidylpeptidase-4 (DPP-4) (e.g. sitagliptin). Of interest, it has been recently reported that such drugs do not only reduce blood sugar levels with favorable effects on lipids and lipoproteins, but also seems reduce cardiovascular risk profile, especially in subjects with type 2 diabetes mellitus (17,18). However, it remains to be fully elucidated in the future whether these agents will be able to benefit clinical cardiovascular outcomes. Interestingly, Berberine, mentioned above, also exerts effects similar to incretins (19).

The European Community has launched several projects in order to reduce the risk from the most common diseases. The Horizon 2020 is a flagship program promoted in Europe in the field of research and innovation, to boost European industry in securing global competitiveness and supporting research and innovation across a range of industries. In particular, this initiative encourages public-private partnerships in research and innovation by helping to provide the resources needed and addressing some of the main challenges in the field of public health. New therapies containing natural products and analogues of substances already present in

our body have been accepted well by patients, and a reduced risk of adverse events has been observed. In fact, the new frontiers of medicine include alternative therapies that hopefully will gradually supplement the current more purely pharmaceutical therapies. Also, many ongoing projects that are aimed at developing new therapeutic strategies for the individual health could lead to a lowering of economic cost and concomitantly reduce overall health risk. One can only wonder if, in this age of facebook and twitter, our grandmothers, by weaving relationships and partnerships with the European Community for the copyright of their ideas, will find all the secrets of their longevity and the elixir of youth revealed in magazines and medical journals.

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## REFERENCES

1. Spitaleri G, Toesca A, Botteri E, Bottiglieri L, Rotmensz N, Boselli S, Sangalli C, Catania C, Toffalorio F, Noberasco C, Delmonte A, Luini A, Veronesi P, Colleoni M, Viale G, Zurrada S, Goldhirsch A, Veronesi U, De Pas T. Breast phyllodes tumor: A review of literature and a single center retrospective series analysis. *Crit Rev Oncol Hematol*. 2013;88(2):427-36.
2. Zeichner SB, Harris A, Turner G, Francavilla M, Lutzky J. An Acquired Factor VIII Inhibitor in a Patient with HIV and HCV: A Case Presentation and Literature Review. *Case Rep Hematol*. 2013;2013:628513.
3. Baicus A. History of polio vaccination. *World J Virol*. 2012;1(4):108-14.
4. Salamone S, Galvano F, Cappello F, Mangiameli A, Barbagallo I, Li Volti G. Silibinin modulates lipid homeostasis and inhibits nuclear factor kappa b activation in experimental nonalcoholic steatohepatitis. *Transl Res June*. 2012; 159(6):477-86.
5. Cacciapuoti F, Scognamiglio A, Palumbo R, Forte R, Cacciapuoti F. Silymarin in non alcoholic fatty liver disease. *World J Hepatol*. 2013; 5(3): 109-113.
6. Ae-Sim Cho a, Seon-Min Jeon b, Myung-Joo Kim c, Jiyoung Yeo d, Kwon-Il Seo e, Myung-Sook Choi b, Mi-Kyung Lee. Chlorogenic acid exhibits anti-obesity property and improves lipid metabolism in high-fat diet-induced-

- obese mice. *Food Chem Toxicol.* 2010; 48(3): 937-43.
7. Bao-Zhu Yu, Rajani Kaimal, Shi Bai, Khalid A. El Sayed, Suren A. Tatulian, Rafael J. Apitz, Mahendra K. Jain, Ruitang Deng, and Otto G. Berg. Effect of Guggulsterone and Cembranoids of *Commiphora mukul* on Pancreatic Phospholipase A2: Role in Hypocholesterolemia. *J. Nat. Prod.* 2009; 72(1): 24-28.
  8. Wang X., Greilberger J, Ledinski G, Kager G, Paigen B, Jürgens G. The hypolipidemic natural product *Commiphora mukul* and its component guggulsterone inhibit oxidative modification of LDL. *Atherosclerosis.* 2004; 172(2): 239-46.
  9. Um MY, Hwang KH, Ahn J, Ha TY. Curcumin Attenuates Diet-Induced Hepatic Steatosis by Activating AMPK. *Basic Clin Pharmacol Toxicol.* 2013; 113(3): 152-7.
  10. Szapary PO, Wolfe ML, Bloedon LT, Cucchiara AJ, DerMarderosian AH, Cirigliano MD, Rader DJ. Guggulipid for the treatment of hypercholesterolemia: a randomized controlled trial. *Jama.* 2003; 290(6): 765-72.
  11. Scotece M, Gómez R, Conde J, Lopez V, Gómez-Reino JJ, Lago F, Smith AB 3rd, Gualillo O. Further evidence for the anti-inflammatory activity of oleocanthal: inhibition of MIP-1 $\alpha$  and IL-6 in J774 macrophages and in ATDC5 chondrocytes. *Life Sci.* 2012;91(23-24):1229-35.
  12. Bennett SM, Hayes JE. Differences in the chemesthetic subqualities of capsaicin, ibuprofen, and olive oil. *Chem Senses.* 2012;37(5):471-8.
  13. Lucas L, Russell A, Keast R. Molecular mechanisms of inflammation. Anti-inflammatory benefits of virgin olive oil and the phenolic compound oleocanthal. *Curr Pharm Des.* 2011;17(8):754-68.
  14. Fogliano V, Sacchi R. Oleocanthal in olive oil: between myth and reality. *Mol Nutr Food Res.* 2006;50(1):5-6.
  15. Rizzo M, Giglio RV, Nikolic D, Patti AM, Campanella C, Cocchi M, Katsiki N, Montalto G. Effects of Chitosan on Plasma Lipids and Lipoproteins: A 4-Month Prospective Pilot Study. *Angiology.* 2013. [Epub ahead of print]
  16. Wang YX, Wang YP, Zhang H, Kong WJ, Li YH, Liu F, Gao RM, Liu T, Jiang JD, Song DQ. Synthesis and biological evaluation of berberine analogues as novel up-regulators for both low-density-lipoprotein receptor and insulin receptor. *Bioorg Med Chem Lett.* 2009;19(21):6004-8.
  17. Rizzo M, Rizvi AA, Spinass GA, Rini GB, Berneis K. Glucose lowering and anti-atherogenic effects of incretin-based therapies: GLP-1 analogues and DPP-4-inhibitors. *Expert Opin Investig Drugs.* 2009;18(10):1495-503.
  18. Rizzo M, Nikolic D, Banach M, Giglio RV, Patti AM, Di Bartolo V, Tamburello A, Zabbara A, Pecoraro G, Montalto G, Rizvi AA. The effects of liraglutide on glucose, inflammatory markers and lipoprotein metabolism: current knowledge and future perspectives. *Clin Lipidol* 2013;8:173-181.
  19. Lu SS, Yu YL, Zhu HJ, Liu XD, Liu L, Liu YW, Wang P, Xie L, Wang GJ. Berberine promotes glucagon-like peptide-1 (7-36) amide secretion in streptozotocin-induced diabetic rats. *Case Rep Hematol.* 2013;2013:628513.
  20. European Commission. Research & Innovation: Horizon 2020. [http://ec.europa.eu/research/horizon2020/index\\_en.cfm](http://ec.europa.eu/research/horizon2020/index_en.cfm).