Supplement to AgroFOOD industry hi-tech - September/October 2010 - vol 21 n 5

Substantiating health claims with research

Notes on the Lycored Science Day 2010

FLORIAN WEIGHARDT
HPC Today
florian@teknoscienze.com

Florian Weighardt

ABSTRACT: From mid of the XIX century on, progress in medicine produced a bulk of evidences on how important correct nutrition is to preserve health and wellbeing. Frequent diseases of the past like gout, scurvy, rickets, beriberi, some forms of anaemia, just to cite a few ones, today, can be prevented by simply adopting an appropriate diet. Since the discovery of the first vitamins made by the polish born biochemist Casimir Funk in 1911, biochemical, physiological and molecular studies have revealed to us the importance of several classes of nutrients and micronutrients not only for the normal housekeeping of physiologic functions but also in preventing severe conditions like cancer or cardiovascular disease. The importance to adopt a correct diet is today a well established concept for everyone. In the last decades a new trend has arisen to supplement and fortify foods and beverages with micronutrients, antioxidants and other categories of important nutrients or to create ex-novo food products designed to achieve beneficial health effects. A number of supplemented and fortified food products, cosmetic products, dietary supplements, drink formulations, etc., are today available promising to the consumers a great variety of advantages for health and wellbeing. In this context the Israel based company Lycored Ltd. produces since 1995 nutrients and nutrient formulations for the food drink and cosmetic industry. The added value Lycored is offering is represented by a solid scientific research backing of its products in all phases of development and testing: a relatively unique feature in the world of nutrients and nutrient formulations. Moreover, the company finances several academic top ranking research groups both to produce sound evidence on the real nutritional features of their products and hints to further enhance them.

THE PROBLEM OF HEALTH CLAIMS

In the sector of food, beverage and cosmetic products, the commercialisation of non pharmaceutical products associated to precise (sometimes exaggerated) health claim has increasingly attracted the attention of control authorities, scientists and consumer protection organisations. In fact, even if scientific evidences exist about the importance of given nutrients for health, this doesn't mean that commercialised supplemented food products, dietary supplements or specific formulations are really useful to consumers. Within this context, official authorities are implementing measures to regulate the field of health claims in order to allow consumers to be correctly informed.

In the European Union a Regulation on nutrition and health claims was issued end of 2006 (EC/1924/2006) laying down harmonised rules for the use of nutrition claims, flanking the rules on food safety already in force. The Regulation foresees that any claim should be clear, accurate and based on evidence accepted by the whole scientific community. Foods bearing misleading or untruthful claims must be removed from the market. Moreover, a register was instituted to keep overview of permitted and rejected claims in the EU.

THE IMPORTANCE OF RESEARCH AND EXPERIMENTATION

Health claims associated to supplemented, fortified or *ad-hoc* developed food or beverage products are of little value if basing only on "paper trails" within scientific literature without any research and experimentation backing them. As every scientist knows, it is not possible to directly transpose even the most solid evidences found in literature into real world without any experimentation. The use of "paper trails" in scientific literature to formulate a novel product represents only the very first part of the development of any novel solution. In addition to that, in most cases, studies found in literature don't share scopes and focuses of who is formulating a new food supplement. As a consequence, data important from the practical point of view may be missing. Studies and experimentations are also necessary to assess and tune crucial aspects like the effective bioavailability of nutrients, their preservation and stability, the avoidance of eventual cross interactions, the determination of correct dosages, etc. In addition to that, often particular technical solutions must be developed to overcome peculiar features of purified nutrients like bad tastes or odours.

It is obvious that food products and beverages, even in the case claims on health and wellbeing are associated to them, are not pharmaceuticals and therefore they need not be tested accordingly. Nevertheless, if health claims are associated to a given product a series of human studies and experimentations have to be performed to substantiate these claims.

LYCORED LTD.

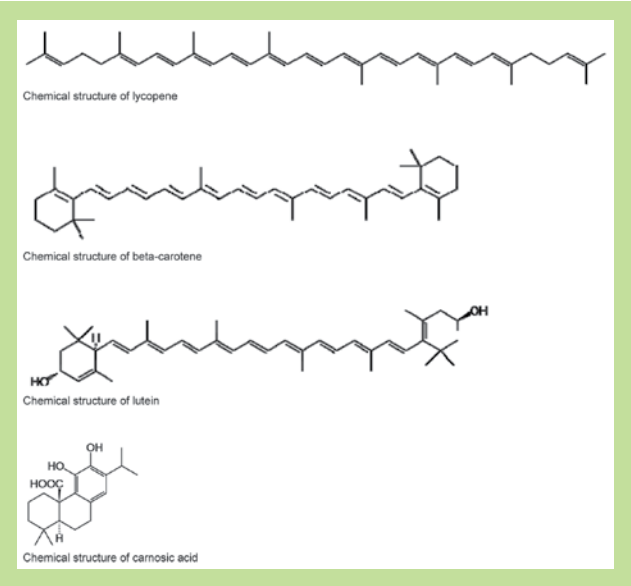
The Israeli company Lycored Ltd. is a global leader in bulk, added-value nutrients for the use in dietary supplements, functional food, beverages and nutri-cosmetics. Lycored's product portfolio includes natural carotenoids (such as lycopene, lutein and beta-carotene) vitamins, minerals, amino acids and other functional ingredients. Moreover, Lycored Ltd. also develops microencapsulated added value food supplements for slow release and improved stability. In addition, the company offers formulations based on natural carotenoids; tomato lycopene, lutein and beta-carotene to be employed as natural food colours. Finally, the company has introduced novel ingredients for the "beauty from inside out" market basing on lycopene, beta-carotene and Lutein.
A distinctive feature of the company resides in its science based approach in developing novel products. This approach is following two directions. On one side Lycored's R&D facilities develop new formulations, procedures, delivery systems and microencapsulation technologies. On the other side, Lycored is financing top ranking academic research groups to conduct focused studies on their products. This way to invest in research not only allows the company to develop and implement their products, but also to get them evaluated by independent (although financed by them) research groups having specific competencies in the field of medical research. The results of some of these researches were presented during a Science Day organised in Tel Aviv (Israel) end of June 2010. The event consisted in two days of presentations and visits to a production plant.

THE LYCORED SCIENCE DAY

The first day of the Lycored science day was dedicated to four scientific presentations held by Rachel Levy (inflammation), Yoav Sharoni (prostate cancer) and Joseph Levy (skin cancer). All three speakers are Professors at the Department of Health Sciences of the Ben-Gurion University of the Negev in Beer-Sheva, Israel. Arnon Aharon, MD, co-founder of a biotechnology consultancy firm, *R&D Integrative Solutions* (Israel) spoke about cardiovascular implications. The second day was dedicated to the worldwide marketing strategies of Lycored Ltd., to the results and to a visit to the tomato fields and a processing plant employed by the company for the first stages of production, which occurs within few hours from the harvest to ensure the best preservation of nutrients.

Anti inflammatory effects
Rachel Levy described in her talk the synergistic anti-inflammatory effects of combinations of lycopene, lutein (both carotenoids) and carnosic acid (a polyphenol). The experiments were carried out using a peritoneal mice macrophage model. Macrophages play an important role in host defence by producing a variety of pro-inflammatory cytokines (e.g. TNFa) and other inflammatory mediators like prostaglandin E2 (PGE_2) and nitric oxide (NO). Attenuation of these inflammatory mediators, involved in the pathogenesis of several human inflammatory diseases, may contribute to anti inflammatory therapies. The study measured the potency of combinations of lycopene, carnosic acid and lutein/beta-carotene in inhibiting inflammatory mediators release triggered by LPS (lipopolysaccharide) exposure. LPS from many bacterial species initiates acute inflammatory responses in mammals that are typical of the host reaction to tissue injury or infection. A pre-incubation of macrophages with blood concentrations of lycopene (1µM), carnosic acid (2µM) and lutein (1µM) or beta-carotene (2µM) before addition of LPS caused an efficient and synergistic inhibition of around 60 percent of NO and PGE_2 production and of 40 percent of TNFa secretion. Instead, addition to media of the single phytonutrients caused only little if no inhibitory effect. Another experiment demonstrated that combinations of the three carotenoids excluding carnosic acid, were less effective, suggesting that the synergistic effect was achieved by combinations of polyphenol and carotenoids. Omitting lycopene from the combination of cartenoids and carnosic acid resulted in a lower inhibition indicating its importance for the process. Rachel Levy suggested that the effect of these phytonutrient combinations is probably due to their anti-oxidant effect. All together these results suggest that blood concentrations of lycopene, carnosic acid and Lutein (or beta-carotene) combinations have a very potent anti-inflammatory effect.

These studies carried out in mice were also confirmed in human white blood cells and human intervention trials are currently underway. Inflammation contributes to a number of chronic conditions like rheumatoid arthritis, myocardial infraction and Alzheimer's disease.



Prostate cancer prevention

Yoav Sharoni made a complete presentation of the state of the art of studies on the effect of carotenoids and lycopene on prostate cancer. In the first part of the talk he presented the data present in bibliography. The epidemiological literature indicates that among 72 studies, 57 reported inverse associations between tomato intake or blood lycopene level and the risk of cancer at a defined anatomic site. The beneficial effect of tomatoes was strongest for cancers of prostate, lung, and stomach. Anticancer properties are best explained by synergic effects among multiple molecules present in tomatoes rather than lycopene alone. In fact, various studies evidence that lycopene alone has virtually no effect on prostate cancer, while whole tomato extracts depict significant effects. Moreover, feeding studies in rats made with combined tomato and broccoli powders demonstrated that the highest decrease in prostate cancer is achieved by the combination of the two ingredients. With regard to the mechanisms involved in anticancer effects for prostate cancer, one study suggests that tomato consumption causes a reduction of serum testosterone, while a study on prostate cancer cells, published by the group of Yoav Sharoni, showed that tomato carotenoids inhibit androgen activity. Based on the results of epidemiological and preclinical studies some intervention studies on prostate cancer patients were carried out with natural tomato preparations. Although more studies are needed to substantiate the role of tomato carotenoids in prostate cancer, existing evidences from preclinical and clinical studies strongly support the reduction of prostate cancer risk by tomato carotenoids. In the same studies it is also evidenced that pure lycopene has a significantly lower effect.

Cardiovascular disease prevention

Arnon Aharon, in his talk, spoke about the effects of anti oxidants, and specifically Lycopene, in the treatment of cardiovascular disease with a special focus on hypertension and atherosclerosis. Hypertension affects, according to estimates, one billion people worldwide and, if not treated, this common disorder can lead to an increase risk of heart attack, stroke and renal failure. Studies were performed by Lycored on the efficacy of a proprietary formulation of concentrated whole tomato extract, Lyc-O-Mato, in reducing blood pressure in three distinct groups: healthy volunteers, individuals with untreated Stage 1 hypertension, and individuals with treated but uncontrolled Stage 1 hypertension. Each of these studies indicates beneficial effect using 15 mg lycopene daily within few weeks of starting dosing (trials were of 8 weeks). Further studies are currently underway.

In the case of artherosclerosis it is well known that antioxidants can inhibit inflammatory process preventing the accumulation of atherosclerotic plaques. Lycored initiated an R&D program that will evaluate its concentrated tomato extract in animal models and human studies on atherosclerosis.

UV photo-protection

Joseph Levy presented the results of his and others studies on UV-radiation photo-protection and skin anti-ageing. Exposure to UV-light causes photo-oxidative reactions that are damaging to the skin with erythema being the initial response. Even if people use sunscreens when deliberately exposing to sunlight it must be considered that in this way only one third of total UV-exposure is covered. Besides classical direct photo-protection achieved with sunscreens, dietary photo-protection is a newly developing concept, even if the protective effect of carotenoids on sun exposure is known since a long time. A direct intervention study on humans demonstrated that both skin density and thickness were increased significantly, with respect to the control group, after 10 weeks of antioxidant mixture supplementation (lycopene, beta-carotene, vitamin E and selenium). In addition to that, roughness and scaling of the skin were improved as well. In another study, individuals supplemented with tomato extract showed protection against sunburn cell formation, while the control group did not. These studies support previous reports demonstrating that tomato antioxidant supplementation diminishes erythema damage from UV A and B radiation. Moreover, they also support the concept that dietary means can protect skin structure and prevent skin aging.

CONCLUSION

Dietary lycopene supplementation alone is not sufficient to achieve its beneficial effect. On the contrary, potent synergic effects are observed when lycopene is administered along with other nutrients or as component of whole tomato extracts. Moreover, during his speech Yoav Sharoni showed a slide in which it was evidenced that plain tomato juice had little or no beneficial effects on prostate cancer prevention, while fresh tomatoes, tomato sauce or pizza had significant effects. This peculiar effect is explainable with the absence of fats in tomato juice. Lycopene is a liposoluble molecule and to be best absorbed with dietary intake (and therefore to be bioavailable) it must be solubilized in a fat (e.g. olive oil). This example alone shows how important research and experimentation are to achieve real efficacy when developing a new product.

Finally, it was also evidenced that to absorb enough lycopene to achieve its several preventive effects through diet, a daily intake of five fully mature (bright red) tomatoes is necessary. Such a high intake is highly improbable also in those countries where tomato is an important component of diet. On the other side formulated supplements (e.g. capsules) contain sufficient concentrated tomato extract to account for the whole required daily uptake

REFERENCES AND NOTES

A full collection of references can be consulted on the scientific reference library of the site of the Lycored company:
http://www.lycored.com/web/content/library.asp