USE OF MICROORGANISMS FOR CAROTENOID DELIVERY: NEXT GENERATION OF PROBIOTICS FOR CARDIOVASCULAR DISEASE

Possemiers S.
ProDigest, Gent, Belgium

Introduction:
Functional foods provide a buoyant growth sector. A particular dynamic area is the use of carotenoids, not only as colorants but also as food additives. One issue with these products is their instability both on the shelf and upon digestion. Specific bacteria from the Bacillus species were shown to produce carotenoids, which have been shown to exert superior stability throughout the gut and higher antioxidant activity and bioavailability than common dietary carotenoids. Furthermore, several Bacillus species have been shown to have probiotic properties, making that the administration of specific carotenoid-producing Bacilli can have unique health benefits. Based on initial promising data, the EU FP7 CARODEL project aimed to reach complete development of an efficient oral delivery strategy of this concept and to evaluate health-beneficial activities of both the carotenoids and the Bacillus delivery vehicle, with the ultimate goal to improve biomarkers associated with cardiovascular disease (CVD).

Methods:
In practice, effective delivery of the carotenoids in the human body was compared upon administration as Bacillus vegetative cells, spores or extracted bacterial carotenoids. In parallel, the ability of the Bacillus strain to exert bona fide effects (i.e. effects on the host microbiota, metabolism and beyond) was investigated using in vitro gut models and in vivo rat studies. Based on this, the best delivery strategy was selected and validated in a 6-week human study, in which carotenoid bioavailability was assessed as well as endpoints related to CVD and probiotic activity. These efforts were combined with a full safety assessment, including 2 phase I human studies, a proof-of-concept production strategy and exploitation plan, to provide a framework for efficient further commercialization of a well-characterized Bacillus carotenoid product.

Results:
Full genomic screening, in vitro and in vivo safety assessment confirmed that the specific Bacillus spores used in this product are safe for human consumption and have an even better safety profile as compared to other Bacilli. Furthermore, safety of oral intake was confirmed in two phase I safety studies conducted in healthy individuals. By combing in vitro gut models and in vivo animal studies, the CARODEL project efforts resulted in an efficient oral delivery strategy of highly active carotenoids, in the form of Bacillus spores, with the additional ability to exert probiotic effects (i.e. effects on gut microbiota, metabolism and beyond). In direct comparison with plant carotenoids, this strategy resulted in superior bioavailability of the bacterial carotenoids, in combination with potent biological effects. The delivery strategy was validated in a 6-week phase II efficacy study in healthy, but overweight individuals. Beneficial effects were observed on biological endpoints after intake of the formulation.

Discussion:
As it was the first time that such effects were shown in humans, the results provide compelling evidence for the further development and commercialization of the CARODEL product as a unique and versatile probiotic.
**Keywords:** Probiotic, Bacillus, Carotenoids, Cardiovascular Disease, Gut Health

**Citation:**