

FUNCTIONAL FOODS: THE BOOM, THE ROADBLOCKS AND THE EVIDENCE

Gone are the days when food was considered a necessity for survival, for satiating hunger or for pleasing the taste buds. The word “food” now triggers off a completely new spectrum of images in one’s mind. With growing awareness and an exponential rise in health consciousness, food is now increasingly associated with its nutritional value, medical benefits and the impetus it can give to one’s overall quality of life. It is this paradigm shift in understanding that has provoked consumers all over the world to look at food as an essential component of healthy life and living. The concept of “Functional Foods” stems from this approach. Food malls, supermarkets, health stores and groceries across the world are now selling a gamut of functional foods ranging from dairy products rich in lactobacillus and cholesterol reducing spreads, to margarine enriched with plant sterols and eggs with enhanced omega 3 fatty acids; just to name a few. The list is indeed endless.

Given this background, it is not surprising that the market size and customer bases for the functional foods industry have grown by leaps and bounds. It is currently an enormous multi billion industry not only in developed nations like the United States, United Kingdom and Japan, but has also witnessed phenomenal growth and acceptance in the South Asian markets of developing countries like India and China. Industry experts strongly opine that a sharp upward movement is expected in this business trend indicating that explosive growth can be expected in the functional foods segment in times to come.

In this context, it would be interesting to note the findings of a market research analysis conducted by Leatherhead, a leading market research firm based in UK¹. Between 2003 and 2010, the global functional food and drink market expanded 1.5 times, with a compounded annual growth rate (CAGR) of 14%, reaching \$24.2 billion USD in 2010. A phenomenal

demand for functional foods has been recorded in the Japanese market followed by the United States and then Europe and Australia. Between 2010 and 2014, Leatherhead predicts a total global market growth of 22.8%, to reach \$29.8 billion by 2014. Dairy products account for a lion's share in the functional foods segment; followed by bakery/cereals, beverages, and fats and oils. In terms of CAGR, however, bakery/cereals are leading (18%), with stiff competition being offered by fats and oils (14%) and dairy (14%). Functional beverages are also growing at 6% CAGR.

However, this remarkable growth journey has been dotted with its own roadblocks. Functional foods are used by consumers without any medical supervision. Often the directions of use, quantities to be consumed per day and conditions of contraindication are not well defined. Very often, functional foods contain components of animal or plant origin which could interfere with drugs that are being taken for treating a disease. For example, several reports poured into the electronic and print media alarming against the indiscriminate use of St. John's Wort enriched functional foods. These reports warned end users about the drug-food interactions noted with the use of St. John's Wort that adversely impacted the bioavailability of drugs being concomitantly taken by patients for serious medical conditions. Botanical extracts such as Ginkgo Biloba, Ginseng and Kava indicated for various health benefits are also known to be associated with horrendous adverse effects such as bleeding and intra cerebral hemorrhages, cardiovascular coagulopathies and extrapyramidal central nervous system effects respectively ².

The current regulations do not mandate the conduct of thorough randomized clinical studies for evaluating the safety and efficacy of functional foods before they are marketed. In some cases and for a few regulators, pre marketing safety studies are required, however, by and large; this market segment remains poorly regulated. In recent times, there has been a growing public and administrative concern regarding this inadequacy in the regulatory framework. Consumers and administrators have now realized that poorly defined

regulations allow marketers of functional foods to make claims that are often unsubstantiated with clinical evidence. End users of functional foods have begun to decipher the fact that very often claims are added onto labels in a very implicit and subtle manner, merely based upon emerging or empirical evidence. Numerous such examples can be cited which lead us to conclude that notwithstanding the commercial surge in the functional foods market, there is also burgeoning concern regarding the unsupervised consumption of these products and the undefined regulatory framework governing this market.

Nevertheless, regulatory authorities across the globe have had to recall several functional food products from the market based upon compelling scientific evidence regarding their unsubstantiated label claims. A couple of examples can be cited in this context. A UK based healthcare giant was entangled in medicolegal complications due to unfounded claims it made over its male dietary supplement containing selenium. The company in question claimed that this supplement potentially reduced the risk for prostate cancer. When found unsubstantiated by regulators, legal action was initiated against the manufacturer in addition to the claim recall. In 2009, the US FDA issued a strict public warning for consumers against the use of Hydroxycut, a weight loss dietary supplement. This warning was issued in response to 23 reports of serious hepatotoxicity associated with the use of this food supplement. In March 2012, the UK's Advertising Standards Agency ordered a UK FMCG major brand to revise a misleading claim mentioned on its website for a cocoa based breakfast cereal. The incorrect claim in question, mentioned that sugar levels were unrelated to obesity and disease development in children. These are just a few randomly chosen examples. Innumerable such other harrowing stories of product and claim recalls of functional foods are abuzz in the media^{3,4}.

In this era of evidence based medicine, randomized controlled clinical and preclinical studies are the gold standards of clinical research and marketing authorizations. Regulators and end users have now begun to realize that it is imperative and prudent to replicate and apply the

“evidence based model” in the realm of functional foods as well. This would ensure that the masses continue to reap the benefits of functional foods under adequately safe and well monitored conditions. Consumer preferences and patterns are changing dramatically. In the wake of safety concerns, aware consumers have now begun to associate the quality of functional foods with the strength of the clinical evidence in favor of the claims made by the manufacturer. In a nutshell, end users have now begun to understand that tall claims made by functional food manufacturers need to be buttressed by equally robust scientific evidence and clinical proof.

Given these changes in consumer preferences and regulatory outlook, there is enough reason to anticipate an increased stringency in the regulatory framework, vis-à-vis the conduct of clinical studies for claim substantiations of functional foods. Current safety concerns prompt us to speculate that large scale, preclinical and clinical randomized well controlled studies would be more frequently required within the functional foods industry. In the light of this regulatory revamp foreseen in the functional foods segment, functional food manufacturers and marketers would need state-of-art facilities and infrastructure to conduct end-to-end rigorous clinical development programs. These programs would comprise of laboratory, animal and human studies for functional foods seeking market authorization.

However, the design and conduct of clinical studies on functional foods presents several scientific, logistic and economic hurdles. Besides budgetary constraints, numerous other obstacles can be identified. There is a long standing dearth of human or animal data regarding the safety and efficacy of functional foods. Needless to say, data emergent from randomized controlled clinical or preclinical studies is most often not available for functional foods. As a result, there is not enough clinical or non clinical evidence that can be utilized for designing a new clinical study.

Therefore, many scientific challenges are encountered while designing a study on functional foods such as deciding the precise patient population, the dosing regimen, choosing the most suitable study design, selecting the comparator whether active or placebo, the sample size, the duration of the study sufficient to elicit a treatment difference, the mechanism of action and the onset and duration of action.

Since functional foods can benefit healthy as well as diseased individuals, the potential study population for studies on functional foods is very diverse and vast. Hence, it often becomes difficult to precisely ascertain the patient population to be chosen for a particular study, since both healthy volunteers and patients could be eligible. This mandates the use of a large sample size for a full-fledged study. Also, short term studies with functional foods may not be able to elicit a “clinically relevant treatment difference”. This is attributable to the fact that functional foods are not medicinal substances. They are natural food products fortified with additional nutrients that give an impetus to health or alleviate disease through natural physiological mechanisms. Thus, longer consistent use would be necessary to witness the health benefits associated with functional foods. Therefore, not only studies with larger sample sizes but also studies of a longer duration would be needed for manifesting the benefits of functional foods in health and disease. This in turn escalates the cost of study conduct.

Most functional foods do not have a scientifically established dosing regimen. Therefore, dose selection for a proposed clinical study becomes difficult. Randomized controlled studies are the gold standard for conducting clinical research. It would be a welcome move to conduct similar randomized studies on functional foods as well. This leaves us with two choices; to conduct randomized controlled studies with an active comparator or with a placebo. With respect to functional foods, problems are encountered with both these options. Owing to lack of clinical evidence with respect to functional foods, a head-on comparative clinical evaluation of the two functional foods becomes difficult. Placebo

controls present logistic difficulties. Since, functional foods are either fortified foods or beverages, it is very cumbersome and at times not possible, to manufacture a matching placebo. Manufacturing such a matching placebo could again have adverse cost repercussions.

In order to better understand the mechanism, onset and duration of action and to obtain information regarding the probable optimal dose to be used in clinical studies; it is advisable to conduct pharmacokinetic and dose-finding in-vitro experiments and animal studies. Small exploratory pilot clinical assessments can then be carried out to determine the sample size and estimate the study duration needed for future larger clinical studies. Improvements in manufacturing technology would have to be accelerated to obtain matching placebos at an economic price. Also, clinically proven information would be needed for potential comparators. These steps would facilitate the conduct of randomized clinical studies with either active or placebo comparators. Large and simple clinical studies with a long follow up could be proposed for assessment of efficacy and safety.

The proposition of generating more and more structured and foolproof clinical evidence, through randomized controlled studies, in the functional foods segment, should be welcomed.

It would certainly be an important milestone in strengthening consumer safety and the commercial interests of manufacturers as well. Clinical research organizations having an excellent track record of conducting similar studies with dietary supplements and other nutraceutical products would certainly play a pivotal role in conducting and managing large scale research projects on functional foods.

So in a lighter vein, the next time you rush to grab your favorite energy booster or your own “low-cal” super cool breakfast cereal.....beware.....read in between the lines.....and be cognizant!!!

References

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