Nutraceuticals pre-clinical research

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A nutraceutical is defined as a “food, or parts of a food, that provide medical or health benefits, including the prevention and treatment of disease”. The definition encompasses medicinal products made from natural ingredients (1).

According to legislation, use of nutraceuticals for health needs to be supported by scientific evidence. Between nutraceuticals and medicinals markets, the fundamental difference is represented by the “intended use” of each category of products. This is “health-keeping” for nutraceuticals and “therapeutic” for medicinal products. Legislation requires scientific demonstration either for both “health keeping” or “therapeutic” intended uses. From this point of view clinical research increased its importance in the last years. However, pre-clinical investigation keeps to be the primary and fundamental proof to address successive research for clinical evidence. Many ingredients of nutraceuticals are food and in consequence they have an adequate safety profile, confirmed by long-term use. But, in cases where a safety concern is recognized or suspected, non-clinical investigations may be needed. The documented experience gathered during the long-standing use generally represents the main basis of the pre-clinical assessment (2). However, particular attention should be paid to effects that are difficult or even impossible to detect clinically. In particular, information coming from preclinical toxicological experiments (i.e., genotoxicity, carcinogenicity, and reproductive studies) is indispensable for safety use of nutraceuticals in humans. Genotoxicity studies are designed to detect genetic damage such as gene mutations and chromosomal aberration, which may reflect teratogenic and tumorigenic potential of substances. Botanical contained in nutraceuticals in the United States are required to provide genotoxicity information prior to marketing approval and recently also European companies of nutraceuticals have increasingly recognized the importance of genotoxic data and consequently have prioritized their acquisition in product development programs. On the basis that genotoxicity studies are highly reproducible, and have high statistical power, by purchasing comparably cost-effective data, companies should be encouraged to realize them as an early goal in their product development. Furthermore carcinogenicity studies should be performed for any product intended for continuous duration of use for more than 3 months or 6 months intermittently. While for shorter term period use, carcinogenicity information could be generally considered less important (3). A crucial issue is represented by nutraceutical ingredients containing chemical compounds that are both genotoxic and carcinogenic. Such compounds include, for example, the allylalkoxybenzenes estragole, methyl eugenol, elemicin, tetramethoxyalkylbenzene, safrole, myristicin, and apiole. Unfortunately, in these cases, assessment of the risk to human health is complicated, and an international scientific agreement concerning the best strategy for the risk assessment of genotoxic and carcinogenic compounds is still lacking. Reproductive toxicity studies are useful to support the safe use of nutraceuticals; however, these studies are not always necessary. This is the case of nutraceuticals which are designed for postmenopausal symptoms or for benign prostate hyperplasia. The only condition for

which there is a cause for concern is for products explicitly indicated in pregnancy. In general, procedures to assess reproductive toxicology should comprise the evaluation of the potential to affect fertility or early embryonic development to implantation, as well as teratology in both a rodent species and a mammalian nonrodent species, and effects on pre- and postnatal development, including maternal function (4). In conclusion, on the basis of the different requirements of scientific proof for nutraceuticals with respect to the medicinal market, also preclinical research should be addressed in the right way. So, for nutraceuticals research should be built with the objective to show that the product is suitable to keep health and not to care for one or more pathologies. Moreover, risks for health such as carcinogenic, mutagenic, teratogenic has to be carefully evaluated.

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4) van den Berg SJ, et al., (2011) Food & Function 2: 760–768.