Problems in the Preclinical Development of Botanical Drugs in Anticancer Therapy

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Cancer is a complex disease, characterized by redundant aberrant signaling pathways as a result of genetic perturbations at different levels. Traditional anticancer therapy involves the use of cytotoxic chemotherapeutic agents, endowed with a relevant toxicological profile and a relatively narrow therapeutic window. Molecularly targeted anticancer therapies are more selective and ideally less toxic than traditional treatments and thus improve tolerability. The inherent plasticity of cancer-cell genetics complicates the development of targeted therapy and secondary mutations or other aberrations may abrogate the effects of targeted agents. Given the complexity and heterogeneity of tumors and the crosstalk among a multitude of signaling pathways, a multitarget approach represents an attractive therapeutic strategy. Botanical drugs are multi-component systems of known and possibly active compounds able to interact with different pharmacologically-relevant targets. Some botanical products are investigative new drug application that have been tested in various phases of clinical trials or are taken out of a patent from single or composite medicinal herbs claiming anticancer properties. However, they are characterized by a number of problems still unresolved. Content variation of products is one of the primary problems with botanical drugs and is a concern about the therapeutic consistency of marketed batches. Furthermore, metabolic interaction with antineoplastic drugs and genotoxic potential are among the most relevant issues, which need to be properly addressed throughout the various phases, preferably earlier phases, of new botanical drug development. Otherwise those issues can pose not only a serious problem to the approvability of those botanical products as new drugs but also a limitation to their post-approval clinical use.