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Computerized quantitative functional dynamics for bio-equivalence & bio-availability

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For chemical and drug entities, whether identical, similar or dissimilar require the priority of determining the mass and chemical structure. The "identical compound" from natural product isolation/purification and from partial/total chemical synthesis are straightforward in bio-equivalence and availability since they share identical physico-chemical properties. For chemical stereo-isomers or synthetic analogs, there are issues of pharmacokinetic (PK) and pharmacodynamic (PD) behaviors: Whether similar, equivalent, or dissimilar, shelf or metabolic stability, salt and formulation, and superior, inferiority or equivalency in effects. PK is well established based on empirical formula and procedures. However, PD assessments are relatively underdeveloped area. This paper is focused on the mass-action law based PD theory, algorithm, experimental design and automated computer simulation that allow efficient, quantitative, and indexed deterministic conclusion for bio-assessments. It allows small size experimentation for econo-green bio-research (Chou TC, Integr. Biol. 3:548-559, 2011). The dose-effect relationships follow the physic-chemical principle of the mass-action law in which the median-effect equation is the unified theory that yields "potency" (Dm value or ED50), "dynamic order" (m value or shape of sigmoidicity) and "conformity" (the r value of the median-effect plot). The usual parameters are the dissociation or affinity constants (K_d or K_a). The new computerized dimensionless parameters/indices are: the Occupancy Index (K_i/IC_{50} ratio), the Therapeutic Index (TD_x/ED_x or the ratio of Toxic and Therapeutic dose ratio), the Combination Index (CI) for drug combination where CI<1, =1, and >1 indicates synergism, additive effect, and antagonism, respectively; the Dose-Deduction Index (DRI) which determines how many fold of dose-reduction is allowed for a synergistic combination. All above constants/indices can be easily quantitatively determined with the CompuSyn software (www.combosyn.com; free download). Proper experimental designs are recommended, and automated simulation can be obtained in 1-2 seconds after data entries, as indicated in Chou TC Pharmacol Rev 58:621-681, 2006. This approach has been proven to have broad applications (Thomson Reuters ISI Web of Science). One article introducing the CI concept (Chou TC & Talalay P, Adv. Enz. Regul. 22-27-55, 1984) has been cited 2,661 times in 523 different biomedical journals (www.researcherid.com/rid/B-4111-2009).

Biography

Ting-Chao Chou received Ph.D. in Pharmacology from Yale University, and Postdoctoral Fellowship at Johns Hopkins University School of Medicine. Joined Memorial Sloan-Kettering Cancer Center (MSKCC), became Member 1988-96, and a Professor of Pharmacology at Cornell University Graduate School of Medical Sciences, 1988-2000. He is Honorary Professor at Chinese Academy of Medical Sciences, Beijing and Visiting Professor at five universities. Currently, he is focusing in the new drug discovery as the Director of Preclinical Pharmacology Core Lab at MSKCC, NYC. His 252 scientific articles are cited over 13,597 times (53.96 citations per article for 252 articles) with H-index of 55. Dr. Chou created the "Unified Theory of Dose-Effect Dynamics of the Mass-Action Law", and with Prof. Paul Talalay (JHU), introduced the "Combination Index Theorem". Seven scientific terms coined by Chou have been widely used. He is Co-inventor of 31 U.S. Patents (top 0.5%-tile of inventors since 1976); several of invented compounds are in clinical trials in cancer patients in U.S.

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