# Screening for nutraceutical-drug interactions toward the noncovalent interactions of their solid binary systems

## (Case study on Piperin)

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The reviled immunomodulating, antioxidant, chemopreventive and anticancer activity of the piperine, mayor alkaloid in fruits of the black pepper (*Piper nigrum* Linn.) and the long pepper (*Piper Longum* Linn.) which for many centuries are broadly used both as spice and as remedy in culinary and traditional medicine, spurs our research on enhancing its low bioavailability.

On a purpose to study interactions between piperine and different pharmacotherapy classes of drugs and other natural compounds with both therapeutic and biological activity that differ by their molecular structures, our initial approach is to apply crystal engineering approach for growing single crystalline phases of cocrystallzed piperin with selected models of drug and natural compounds. Referring to the ternary amide structure of piperine which is formed between piperidine in chair conformation and piperic acid (5-(3,4-methylenedioxyphenyl)-2,4-pentadienoic acid), its side chain with conjugated double bonds impacts to the appearance of piperine in four possible geometric isomers [1,2]. We envisage that structural flexibility of piperine is favourable for forming amide-amide type of non-covalent H-bond interactions with drugs (e.g. secondary amide moiety in molecule of perindopril – ACE inhibitor, tertiary amide in prazosin- α-adrenoceptor antagonists, primary amide in carbamazepine – antiepileptic drug and etc. ) and for forming amide-catvoxylate and amide-hydroxyl H-bonding interaction with drugs and natural compounds (e.g. ascorbic acid with enediole structure and curcumine with β-diketo and hydroxyl benzoic moieties in its structure).

Regarding to our previously resolved structure of cocrystalized curcumine with ternary N-compound (not yet published) we present case study of solid binary systems containing piperine in combination with drugs and natural compounds with therapeutically activity.

Spectroscopic (FR-IR, Raman), Thermal (DSC-TG) and powder R-ray diffraction analyses confirms the H-bonding interactions and resolved structures reveal the patterns of packing and directionality of the interaction in crystal structure that offer opportunity to predict the mode of interactions of piperine in *in vivo* testing.

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