7 natural products viz. withaferin, podophyllotoxin, 3-demethylcolchicine, agnuside, reserpine, seseberecine and fascaplysin as P-gp inducers. Fascaplysin (6a), a marine-derived bis-indole alkaloid, was the most potent among all of them, showing induction of P-gp with EC50 value of 25 nM. P-gp induction is one of the recently targeted strategy to increase amyloid-beta clearance from Alzheimer brains. Thus, we pursued a medicinal chemistry of fascaplysin to establish its structure-activity relationship for P-gp induction activity. Four series of analogs viz. substituted quaternary fascaplysin analogs, D-ring opened quaternary analogs, D-ring opened non-quaternary analogs, and beta-carbolinium analogs were synthesized and screened for P-gp induction activity. Among the total of 48 analogs screened, only quaternary nitrogen containing analogs 6a-g and 10a, 10h-l displayed promising P-gp induction activity; whereas non-planar non-quaternary analogs 9a-m, 13a-n, 15a-h were devoid of this activity. The P-gp induction activity of best compounds was then confirmed by western-blot analysis, which indicated that fascaplysin (6a) along with 4,5-difluoro analog of fascaplysin 6f and D-ring opened analog 10j displayed 4–8 fold increase in P-gp expression in LS-180 cells at 1 μM. Additionally, compounds 6a and 6f also showed inhibition of acetylcholinestease (AChE), an enzyme responsible for neuronal loss in Alzheimer's disease. Thus, fascaplysin and its analogs showing promising P-gp induction along with AChE inhibition at 1 μM, with good safety window (LS-180: IC50 > 10 μM, hGF: 4 μM), clearly indicates their promise for development as an anti-Alzheimer agent.

Mann, A. K. P. et al. (2018). "Producing amorphous solid dispersions via co-precipitation and spray drying: Impact to physicochemical and biopharmaceutical properties." *J Pharm Sci* 107(1):183–191.

Many small-molecule active pharmaceutical ingredients (APIs) exhibit low aqueous solubility and benefit from generation of amorphous dispersions of the API and polymer to improve their dissolution properties. Spray drying and hot-melt extrusion are 2 common methods to produce these dispersions; however, for some systems, these approaches may not be optimal, and it would be beneficial to have an alternative route. Herein, amorphous solid dispersions of compound A, a low-solubility weak acid, and copovidone were made by conventional spray drying and co-precipitation. The physicochemical properties of the 2 materials were assessed via X-ray diffraction, differential scanning calorimetry, thermal gravimetric analysis, and scanning electron microscopy. The amorphous dispersions were then formulated and tableted, and the performance was assessed in vivo and in vitro. In human dissolution studies, the co-precipitation tablets had slightly slower dissolution than the spray-dried dispersion, but both reached full release of compound A. In canine in vitro dissolution studies, the tablets showed comparable dissolution profiles. Finally, canine pharmacokinetic studies showed that the materials had comparable values for the area under the curve, bioavailability, and Cmax. Based on the summarized data, we conclude that for some APIs, co-precipitation is a viable alternative to spray drying to make solid amorphous dispersions while maintaining desirable physicochemical and biopharmaceutical characteristics.

Miao, Y. et al. (2016). "Characterization and evaluation of self-nanoemulsifying sustained-release pellet formulation of ziprasidone with enhanced bioavailability and no food effect." *Drug Deliv* 23(7):2163–2172.

The purpose of this work was to develop self-nanomulsifying drug delivery systems (SNEDDS) in sustained-release pellets of ziprasidone to enhance the oral