Reactive Oxygen Scavenger Effect of Pyrimidines, Benzotriazoles and Related Compounds

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Abstract

Free radicals and reactive oxygen metabolites have been implicated as important pathologic mediators in many clinical disorders and diseases. An efficient method of detecting the free radical scavenger effect is through xanthine oxidase (XO) inhibition. The inhibition efficiency on XO has been detected as the rate of uric acid production, which has max 295 nm. Sulfasalazine showed potent inhibiting activity on XO (IC50 = 25.11 microM; Ki = 50.88 microM) and induced a mixed-type (non-competitive-uncompetitive) inhibition of the substrate xanthine. 2-mercapto-4(3H)-quinazolinone (16) and 2-mercaptopyrimidine (4) displayed inhibiting activity on XO with IC50 = 98.71 and 136.14 microM, while apparent inhibition constants (Ki) were 158.38 and 62.46 microM, respectively. However benzotriazoles showed weak inhibitory effect. The spin-trapping method with 5,5-dimethyl-1-pyrroline N-oxide (DMPO) by electron spin resonance (ESR) detected the presence of O2-* and OH*. It showed that the percentage inhibition for formation of DMPO-OOH for 2-mercapto-pyrimidine and sulfasalazine were 64.78 and 35.09, but for hydroxylation were 49.51, 38.55, 37.29 for 2-mercapto-4(3H)-quinazolinone, sulfasalazine and 2-mercaptopyrimidine at 500 microM, respectively.