Safe Improvement of Drug Absorption by Combinatorial Use of Sodium Laurate with Amino Acids

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Development of combinatorial chemistry and high-throughput screening technique has made it possible to generate a lot of new drug candidates very rapidly, but it has resulted in a number of poorly soluble and/or poorly absorbable candidates. A new trend of drug development based on pharmacogenomics or development of molecular targeted drug is also spurring the tendency, and it does not necessarily lead to good output in terms of the development of new drugs. It is very attractive to improve the membrane permeability as well as the solubility by using some adjuvants, because the method can be applicable for various drugs. However, the practical use of the absorption-enhancing adjuvants has been very limited because of the potential local toxicity. Therefore, suppressing the potential local toxicity would lead to the successful development of safe preparation that can improve the absorption by using adjuvants. Our biochemical and histopathological studies showed that several amino acids such as taurine (Tau) and L-glutamine had cytoprotective action, and it has been found that the combinatorial use of sodium laurate (C12) with these amino acids could maintain the absorption-enhancing ability of C12. Suppository preparation containing C12 and Tau remarkably improved the rectal absorption of rebamipide, classified into BCS Class IV, and the preparation was quite safe to the rectal mucosa. As for the mechanisms of cytoprotective action by these amino acids, it has been found that these amino acids could suppress the intracellular calcium level, induce the expression of heat shock protein 70 and suppress the release of histamine.