

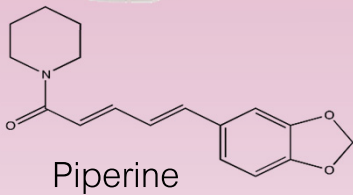
Drug discovery for cholera using chemicals derived from natural resources

Secretory diarrhea

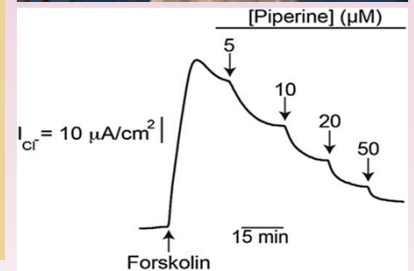
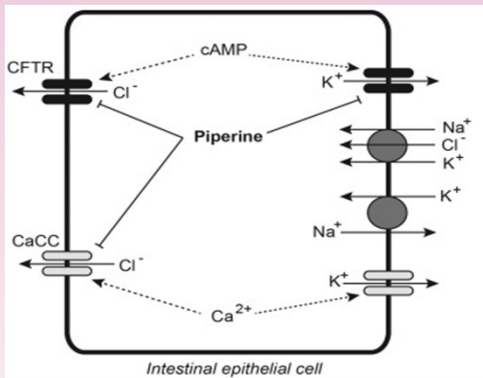
Secretory diarrhea is a leading cause of morbidity and mortality worldwide, especially in children under 5 years of age. It is mainly caused by intestinal infection with pathogenic bacteria such as *Vibrio cholerae* and *Escherichia coli*. Indeed, pathophysiology of these secretory diarrheal diseases involve enterotoxin-induced hypersecretion of chloride in intestinal epithelial cells, which drives massive fluid loss causing severe dehydration and death. In case of cholera, cholera toxin is a major virulence that causes hyperactivation of the cystic fibrosis transmembrane conductance regulator (CFTR) chloride channel which provide driving force that drive fluid secretion. Therefore, inhibition of CFTR and other chloride channels are proposed to be the promising targets for the treatment of secretory diarrhea in cholera. In the nature, several types of herb are known to produce an anti-diarrheal effect such as black pepper. Importantly, it is therefore interested to study the effects of black pepper and its ingredients in the diarrheal model. In mechanistic study, we also investigate effects of ingredients from black pepper on CFTR activity.



Black pepper



Piperine



Black pepper and piperine

Black pepper has long been in the traditional anti-diarrheal regimens. However, mechanisms underlying its anti-diarrheal efficacy is unknown. This study is to investigate the effects of piperine, the main ingredient of black pepper, on CFTR chloride channel activity, and its anti-diarrheal effect. It was found that black pepper and piperine effectively inhibited CFTR activity. Interestingly, piperine also suppressed cholera toxin-induced intestinal fluid secretion in cholera mouse model. Taken together, these results indicates that piperine represents a novel class of drug candidates for the treatment of diarrheal diseases caused by the intestinal hypersecretion of chloride.

Application for diarrhea

In conclusion, we provide an evidence showing *in vivo* anti-diarrheal effect of piperine and its underlying mechanisms at molecular and cellular levels. Therefore, based on our finding, it may lead to the successful development of effective anti-diarrheal drug from inexpensive natural product such as black pepper. Since pepper black can be purchased from a local market, especially in Thailand, we also used the black pepper for the prevention or treatment of diarrheal diseases caused by pathogenic infection such as *Vibrio cholerae* and *Escherichia coli*. However, we also need the evidence from human or clinical trials in order to be sure in the anti-diarrheal effect of black pepper and its main ingredient piperine.



Control

Cholera toxin (CT)

CT + Piperine

