

## Relationship between autophagy and apoptosis of menthol-induced cytotoxicity in lung cancer cell line, A549

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Menthol, a cooling inducer, is known to be an agonist of TRPM8 and TRPA1. It has beneficial effects such as analgesic and anti-inflammatory actions in lung and skin. Previously, we demonstrated that menthol induced mitochondria dysfunctions resulting in caspase-dependent apoptosis, thus menthol possesses the cytotoxicity in lung cancer cell line, A549. However, effect of menthol on an autophagy, an another cellular response, is unclear. The expression of molecules related to autophagy was detected by using western blotting. Flow cytometrical analyses were performed to detect apoptosis. Menthol (2 mM) induced the increases of LC3 type II, an autophagy-related molecule. Chloroquine, an inhibitor of lysosomal function, enhanced the level of LC3 type II indicating that menthol elicited the autophagy. Menthol-induced apoptosis was enhanced by chloroquine. Caspase inhibitors failed to block the apoptosis induced by the combination of menthol and chloroquine. These results suggest that menthol induces autophagy which plays a role for cell survival in A549. Use of menthol together with chloroquine may be a novel therapeutic strategy for lung cancer diseases.