

7-Methoxyheptaphylline Sensitizes TRAIL-induced Colorectal Adenocarcinoma Cells Death through Up-Regulation of DR5 Expression by Activation of JNK



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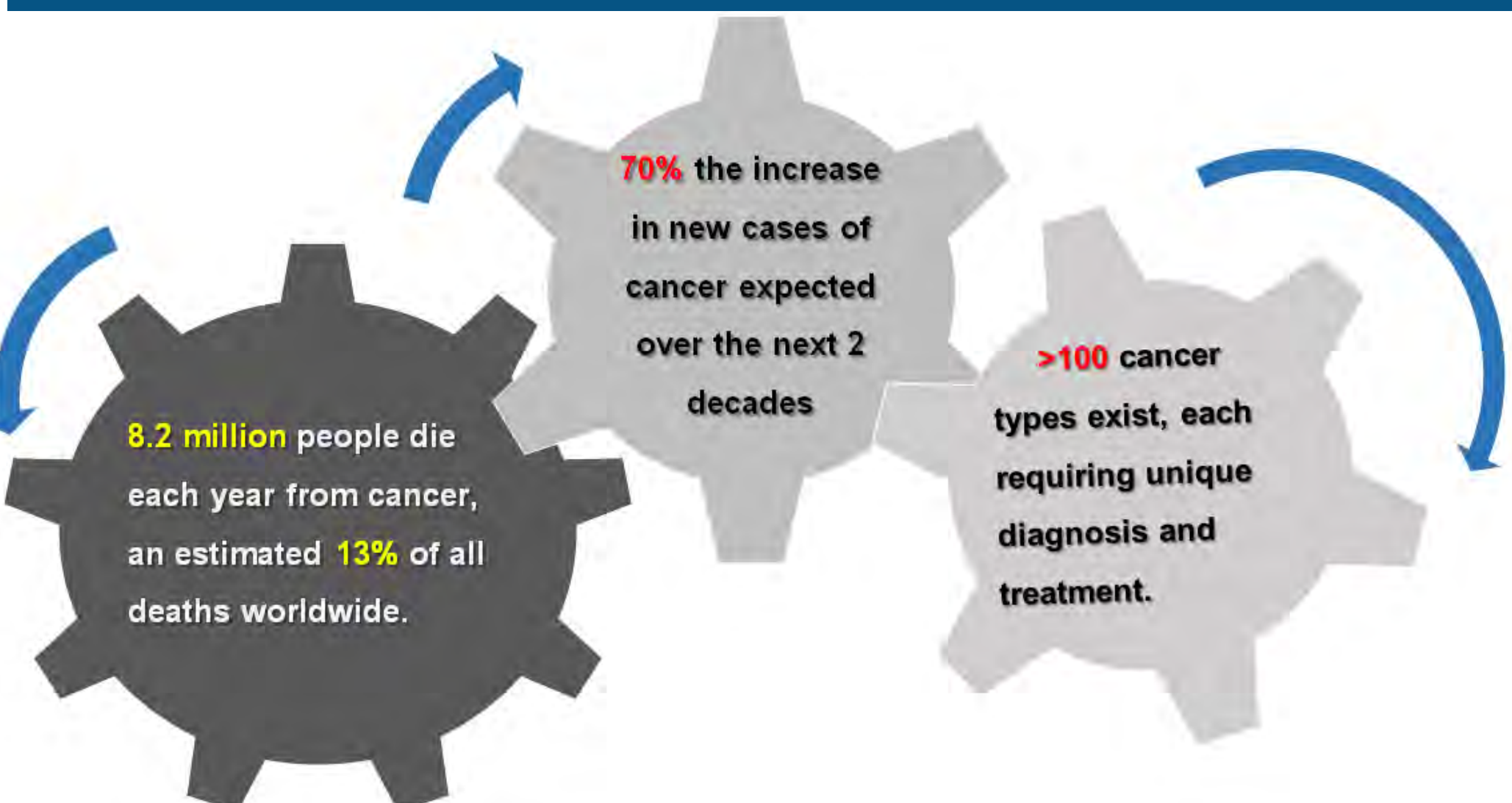
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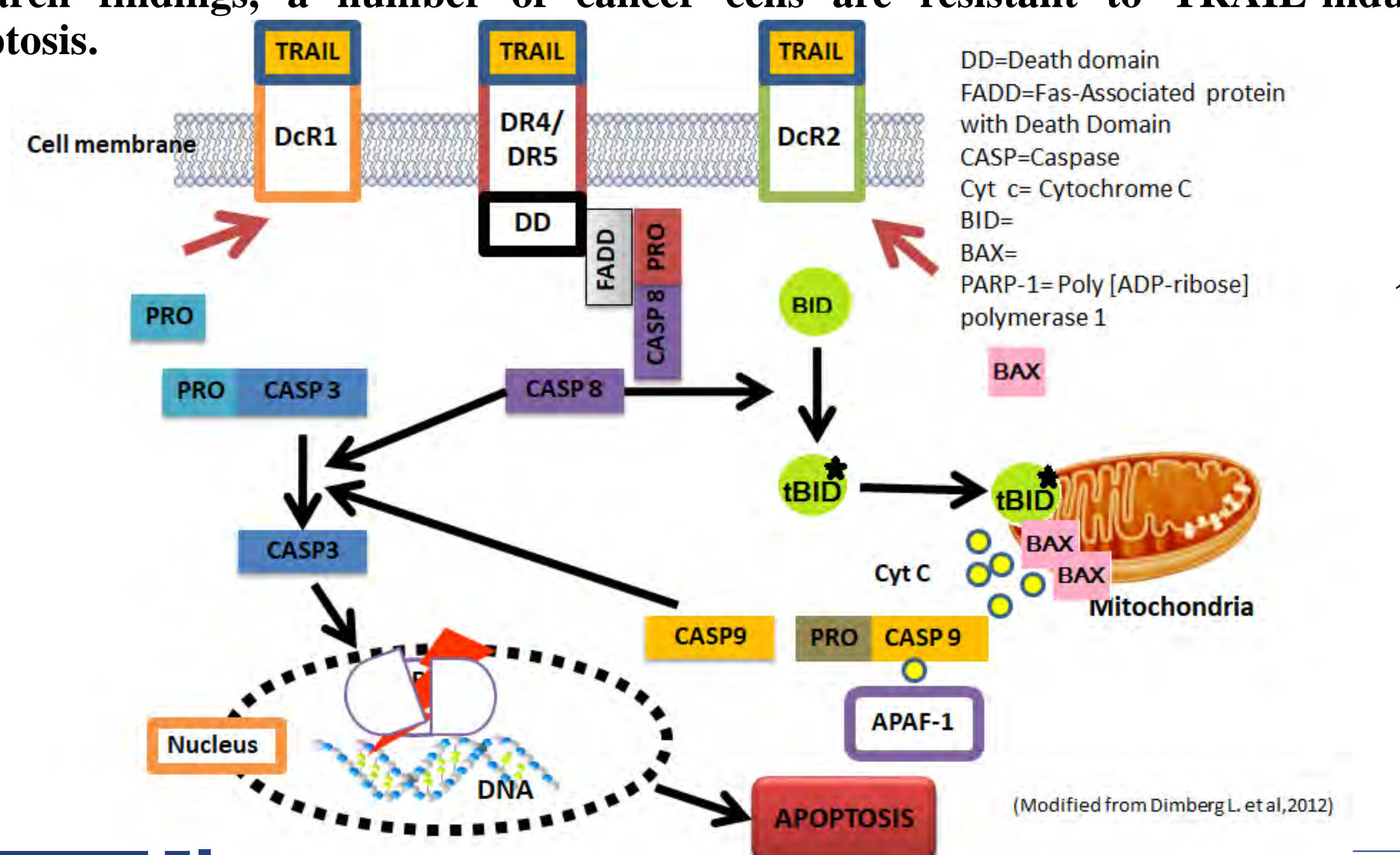
Cancer



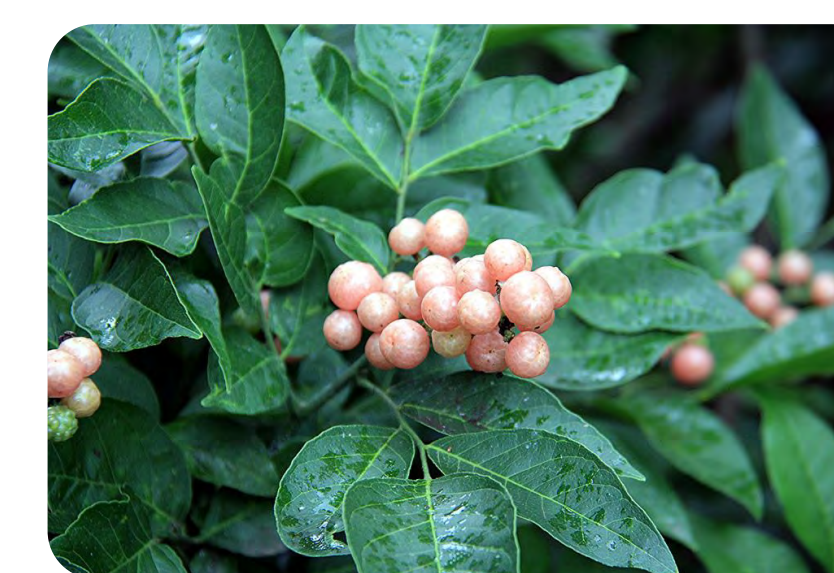
This study aimed to investigate the effect of carbazole derivatives, including heptaphylling and 7-methoxyheptaphylline from *Clausena harmandiana* on TRAIL-induced colon adenocarcinoma (HT-29) cell death

Signaling molecules related cancer and alzheimer's disease

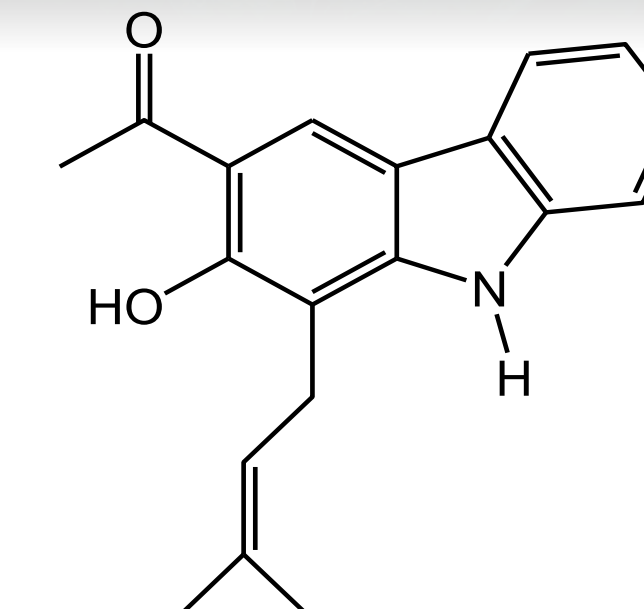
TRAIL (TNF-related apoptosis inducing ligand) is a cytokine that can selectively induce apoptosis in cancer cells without damaging normal cells. Regarding current research findings, a number of cancer cells are resistant to TRAIL-induced apoptosis.



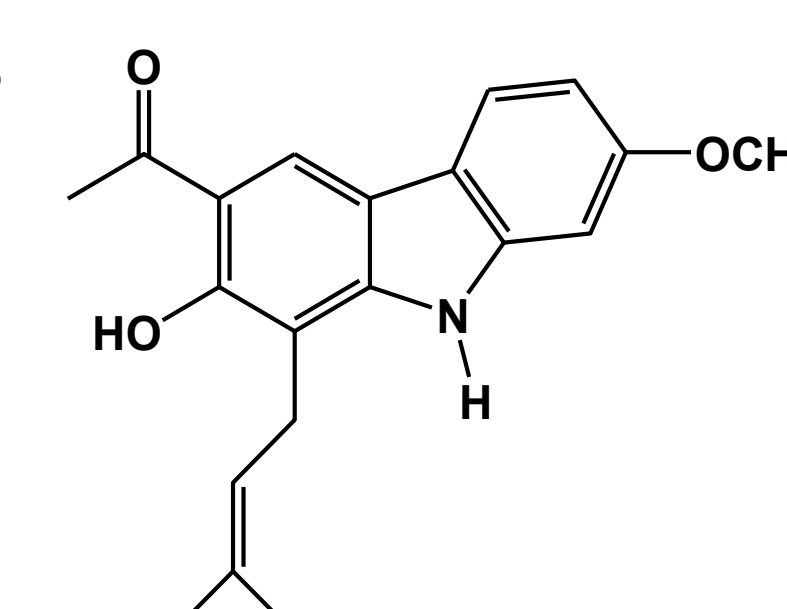
Clausena harmandiana



- Clausena harmandiana* known as "Song Fa"
- Family: Rutaceae
- Distribution: Southeast Asia
Thailand: Northeastern part.
- Young leaves are used by humans for food and as medicinal plant.
- Roots have been used as a folk remedy medicine.
- Treatment: headache, fever bronchitis and abdominal discomfort.



Heptaphylline

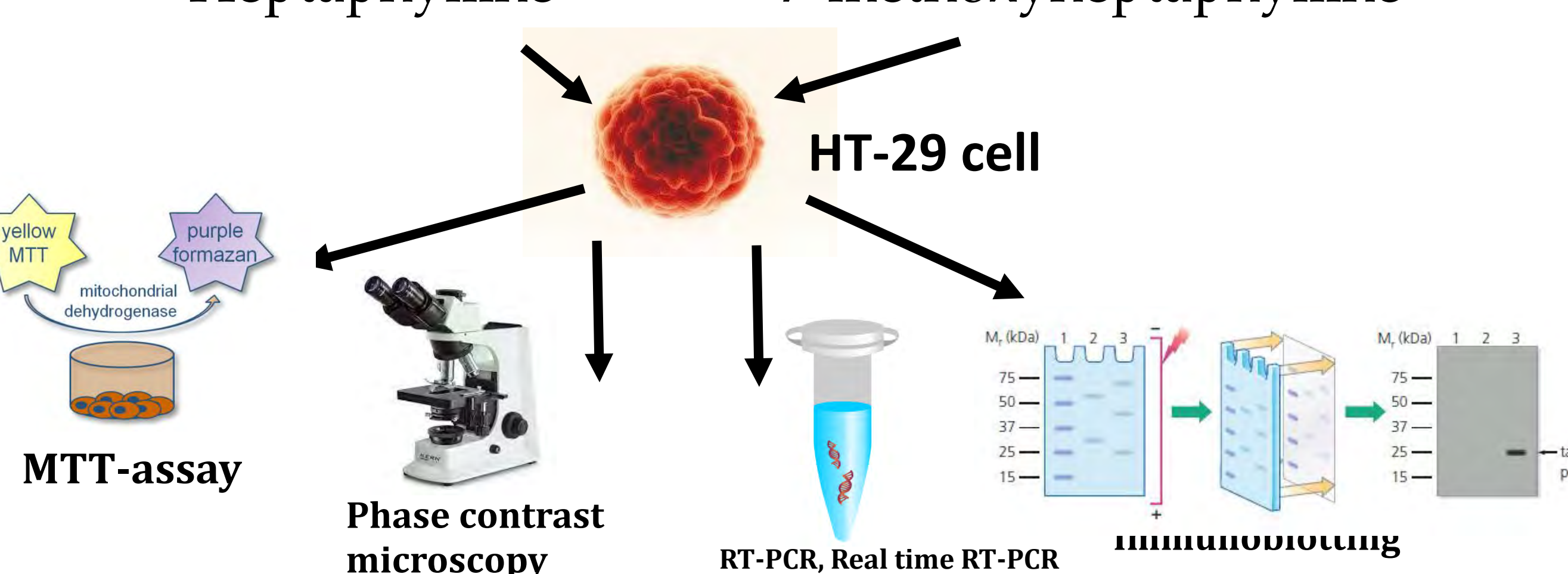


7-methoxyheptaphylline

The structures of heptaphylline and 7-methoxyheptaphylline.

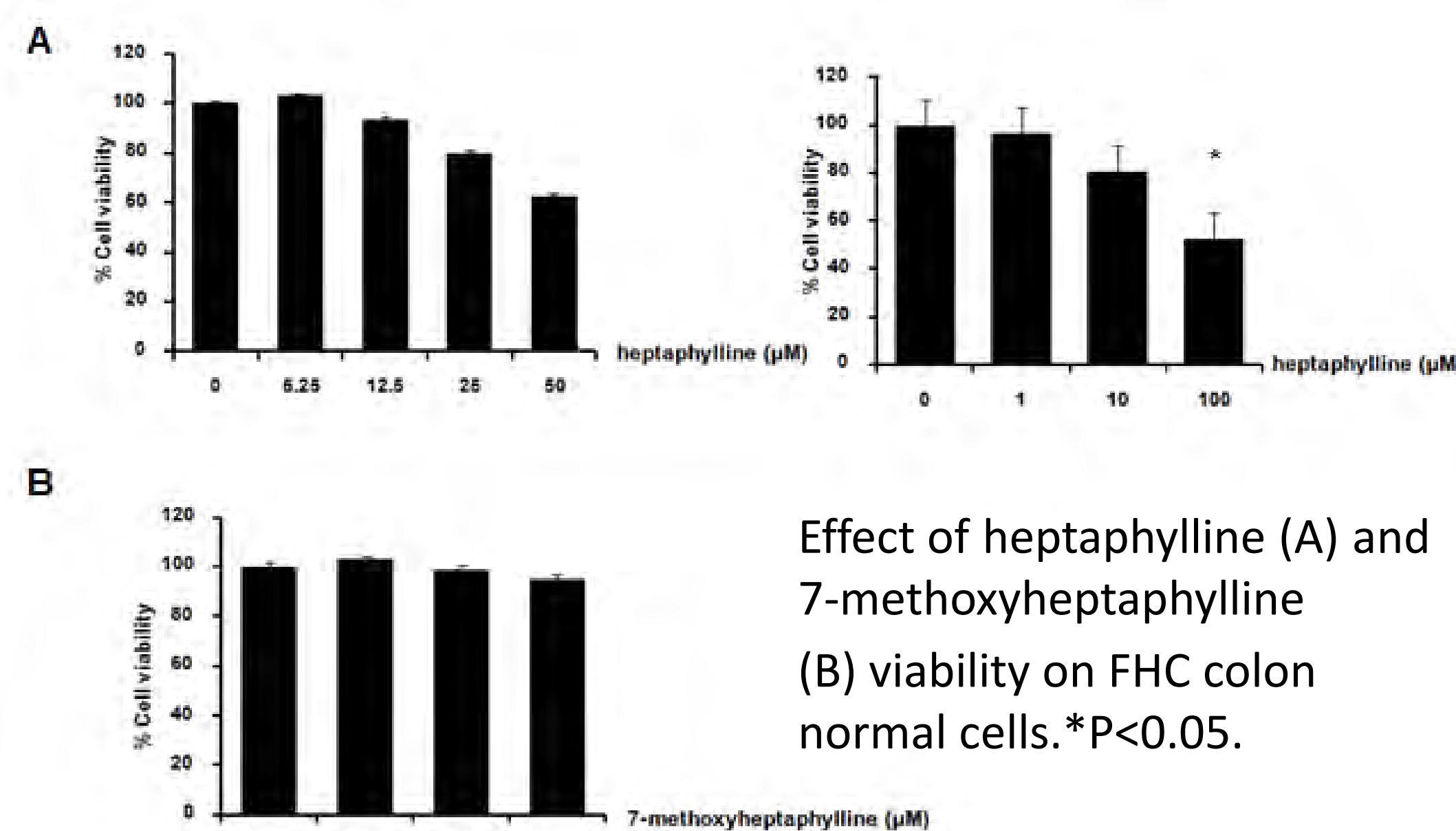
Methods

- Test compounds: heptaphylline, 7-methoxyheptaphylline
- Cell viability: MTT-assay
- Cell morphology: Phase contrast microscopy
- mRNA expression: RT-PCR, Real time RT-PCR
- Protein expression: Immunoblotting

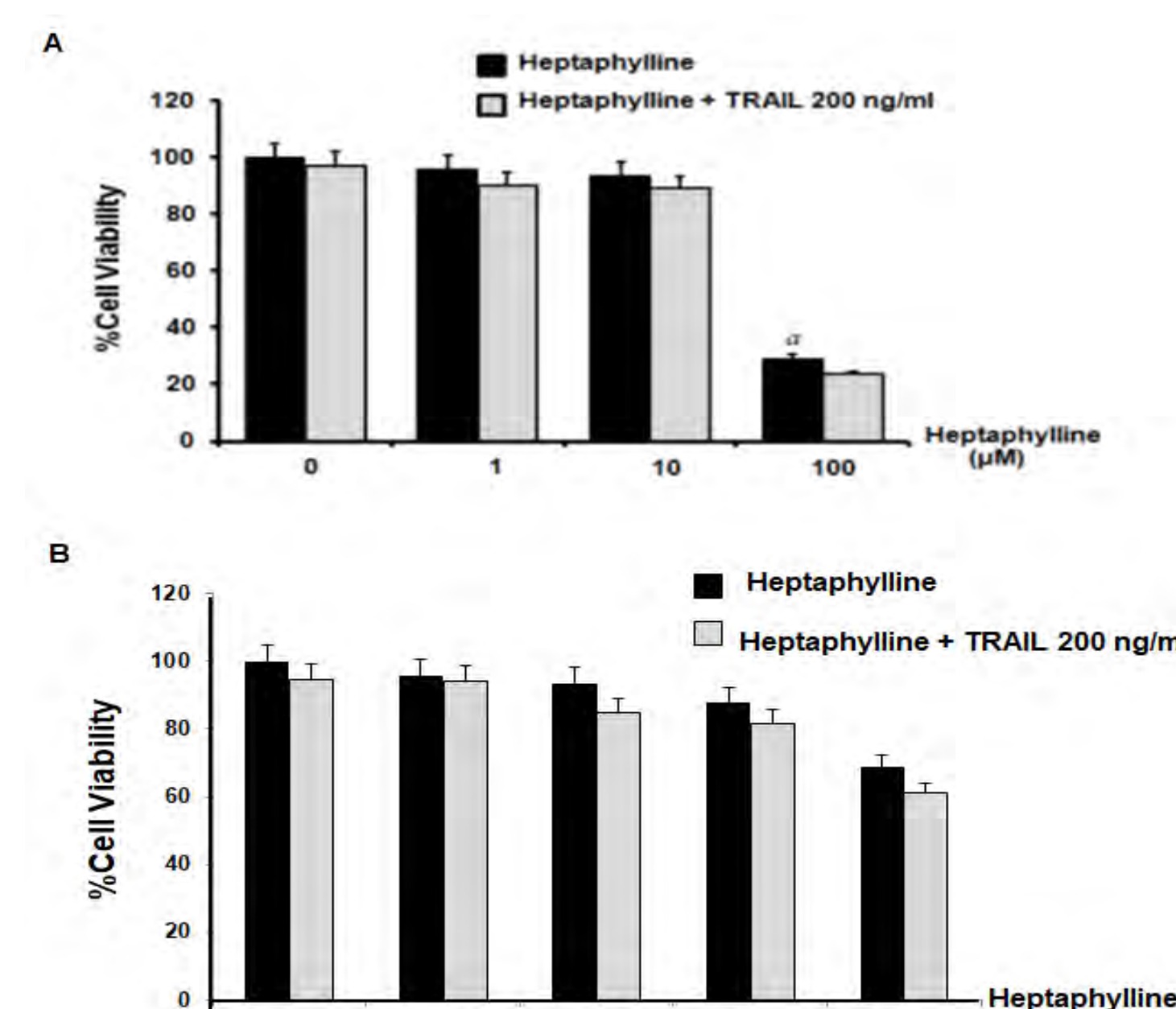


Results

Cytotoxic effect of heptaphylline and 7-methoxyheptaphylline on FHC colon normal cell



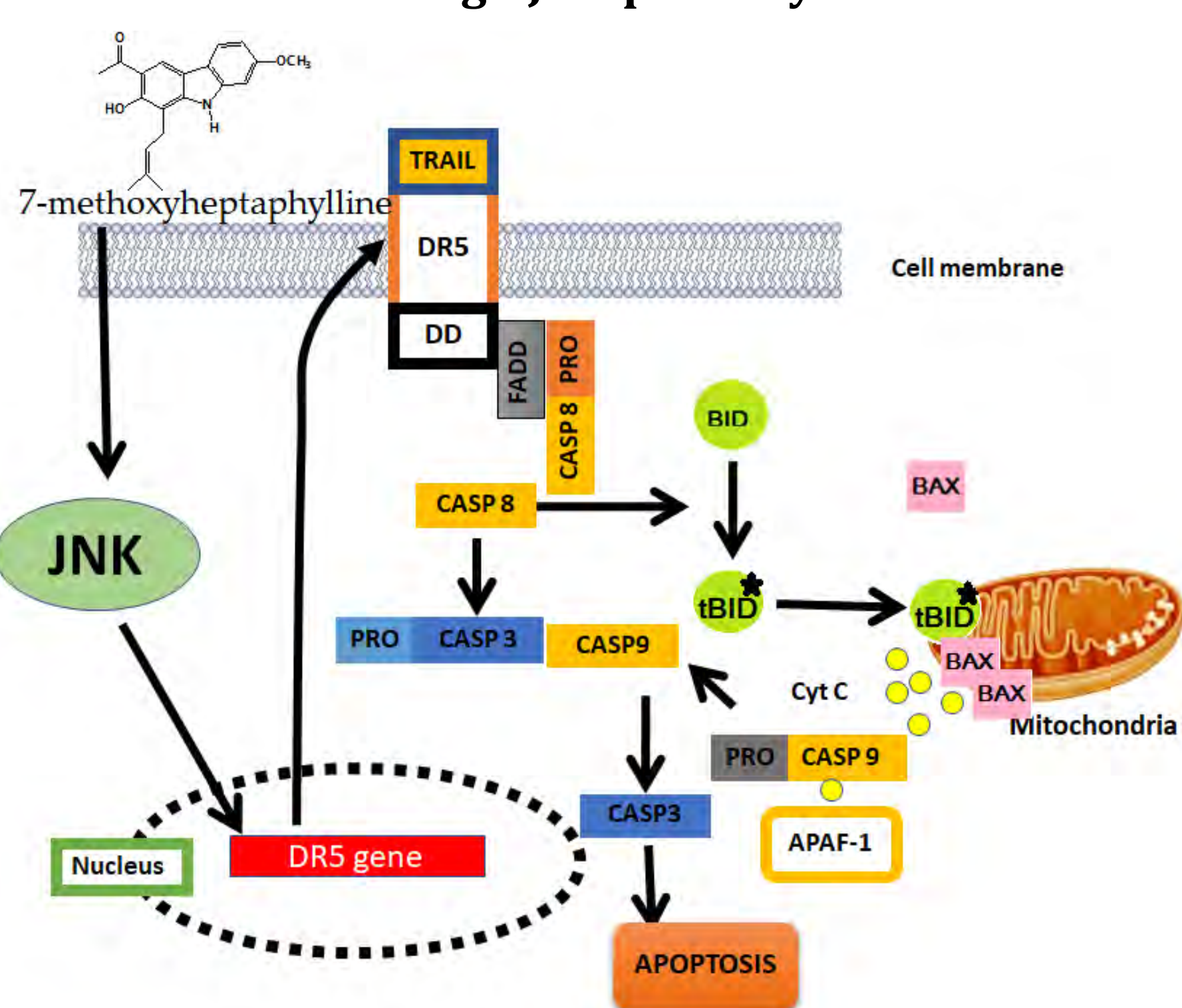
Cytotoxic effect of heptaphylline and 7-methoxyheptaphylline on FHC colon normal cell



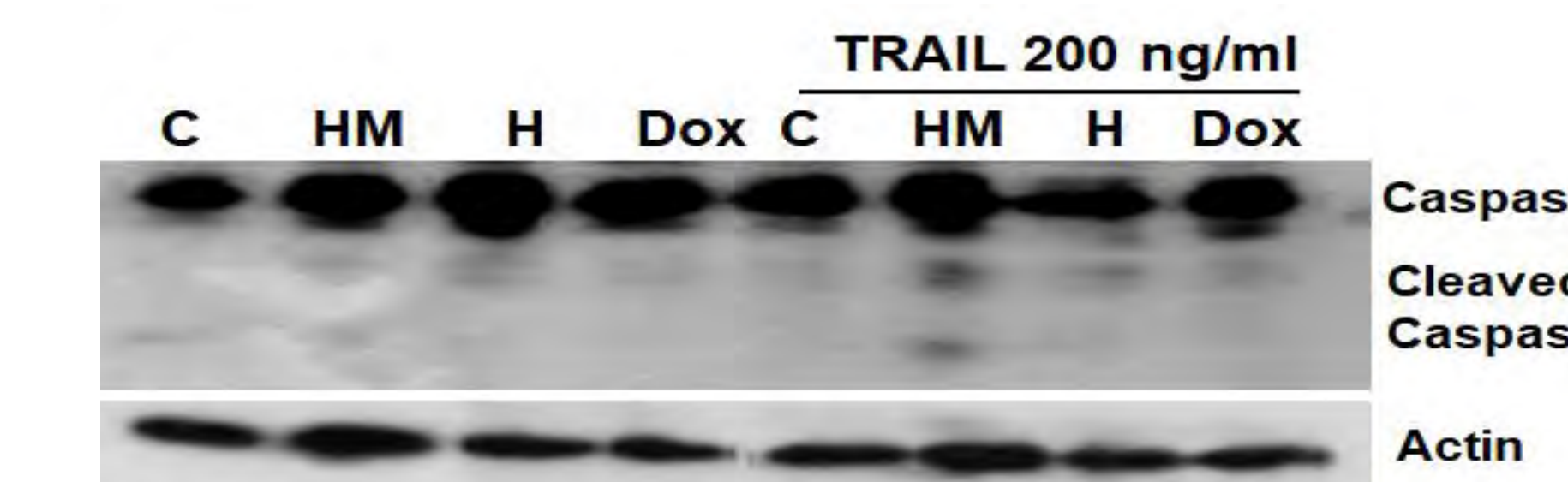
Effect of 7-methoxyheptaphylline on HT29 cells and TRAIL-induced HT29 cells. n=3, ^a p < 0.01, ^{aa} p < 0.001, ^a comparing between cells treated with 7-methoxyheptaphylline and control, ^b comparing between cells treated with 7-methoxyheptaphylline combined with TRAIL.

Conclusion

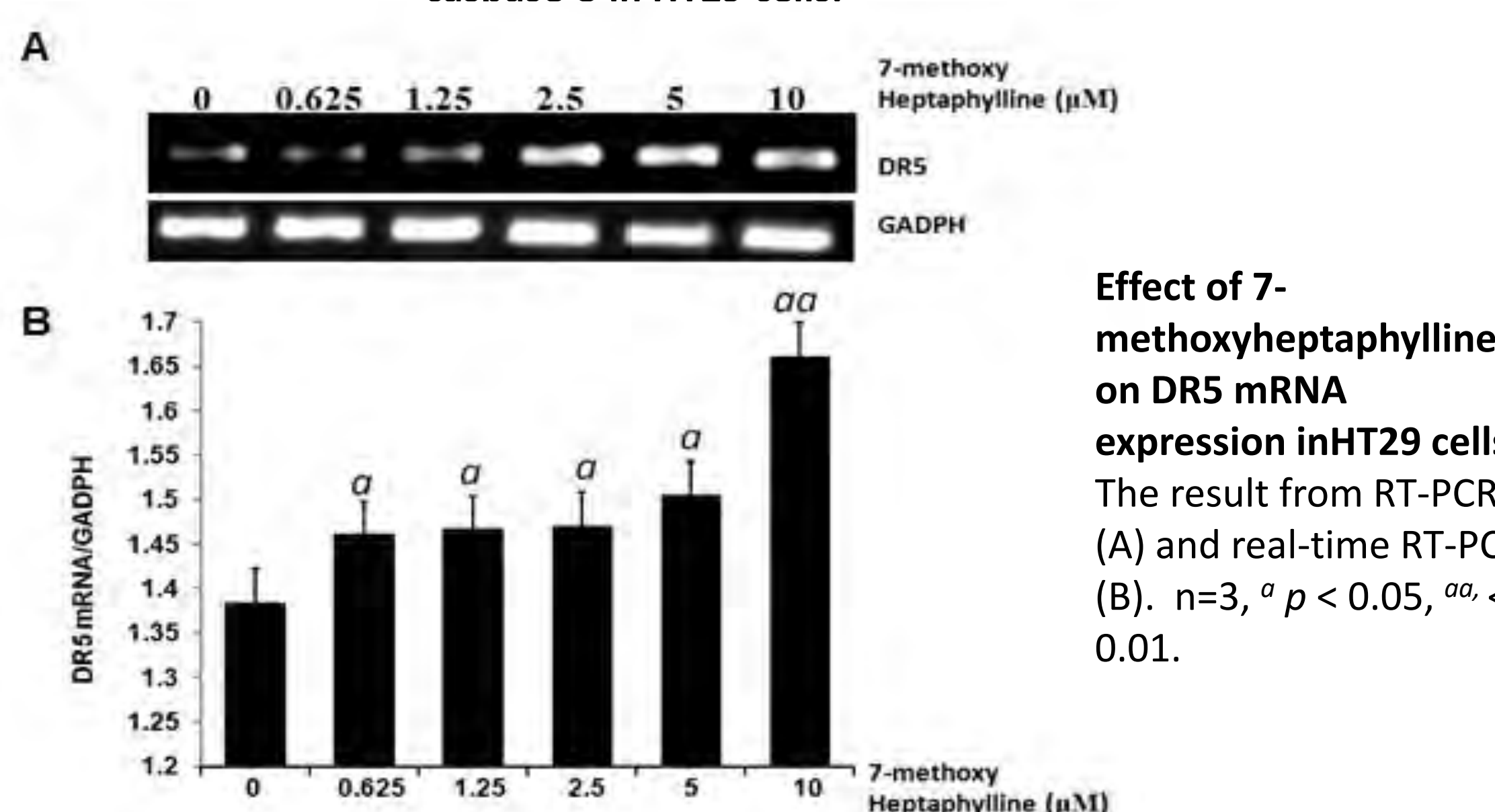
This study indicated that 7-methoxyheptaphylline, a carbazole derivative enhanced TRAIL-induced HT-29 colon adenocarcinoma apoptosis by increased level of DR5 through JNK pathway



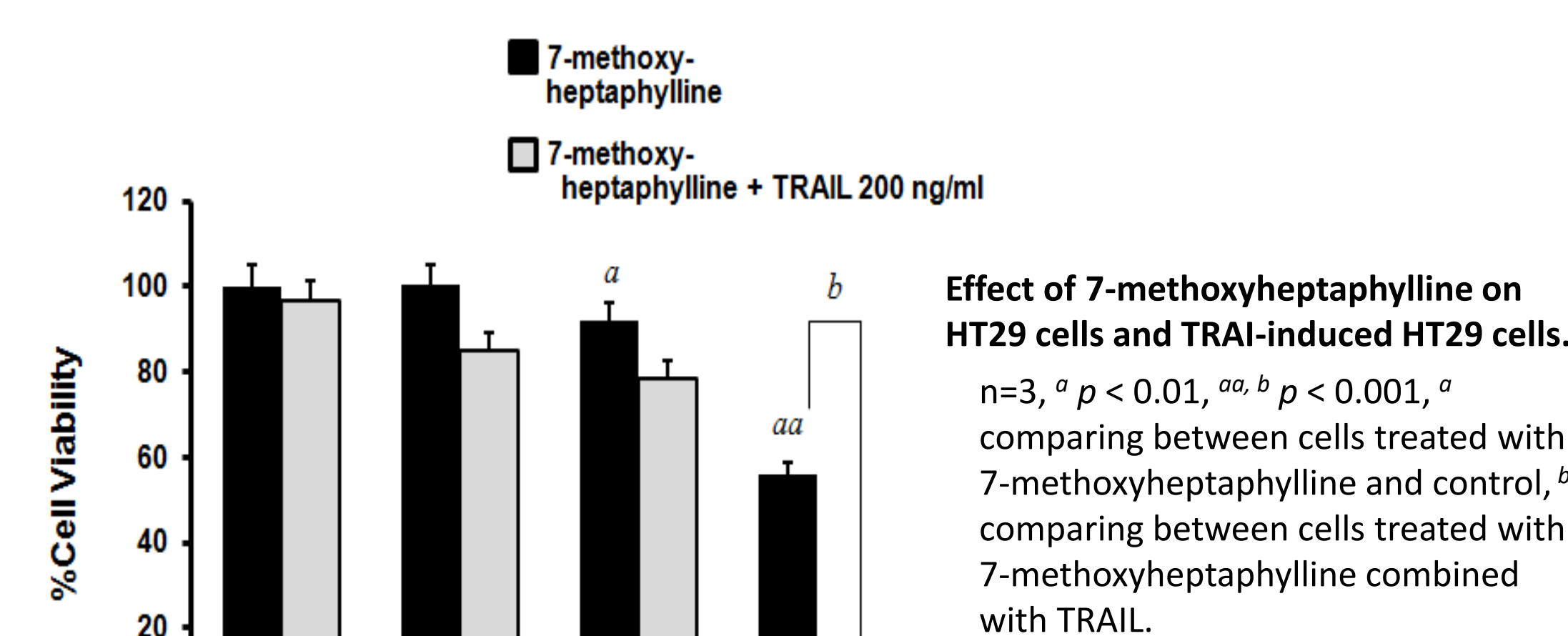
7-methoxyheptaphylline enhanced TRAIL-induced HT29 cancer cell apoptosis through increasing DR5 level



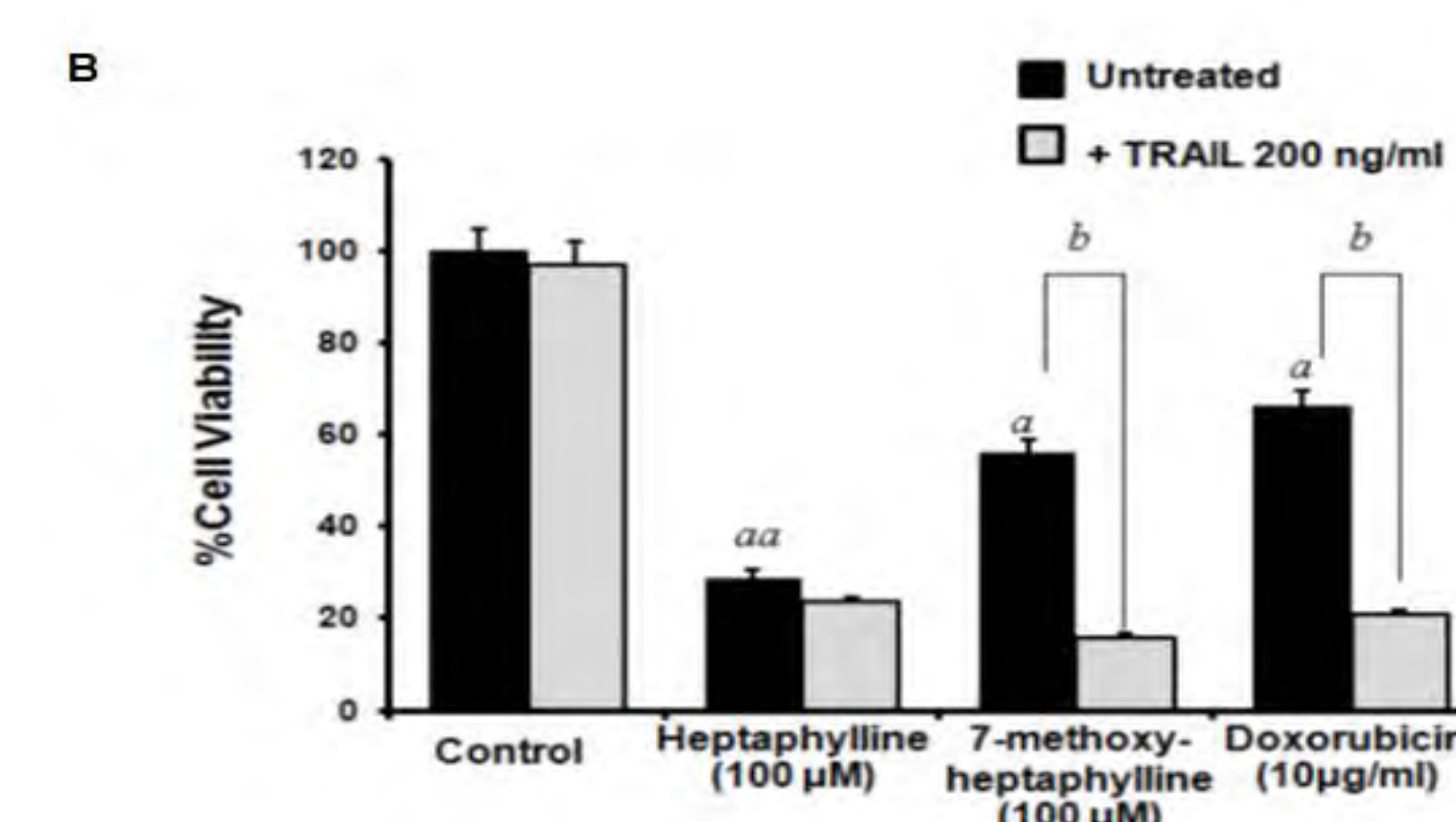
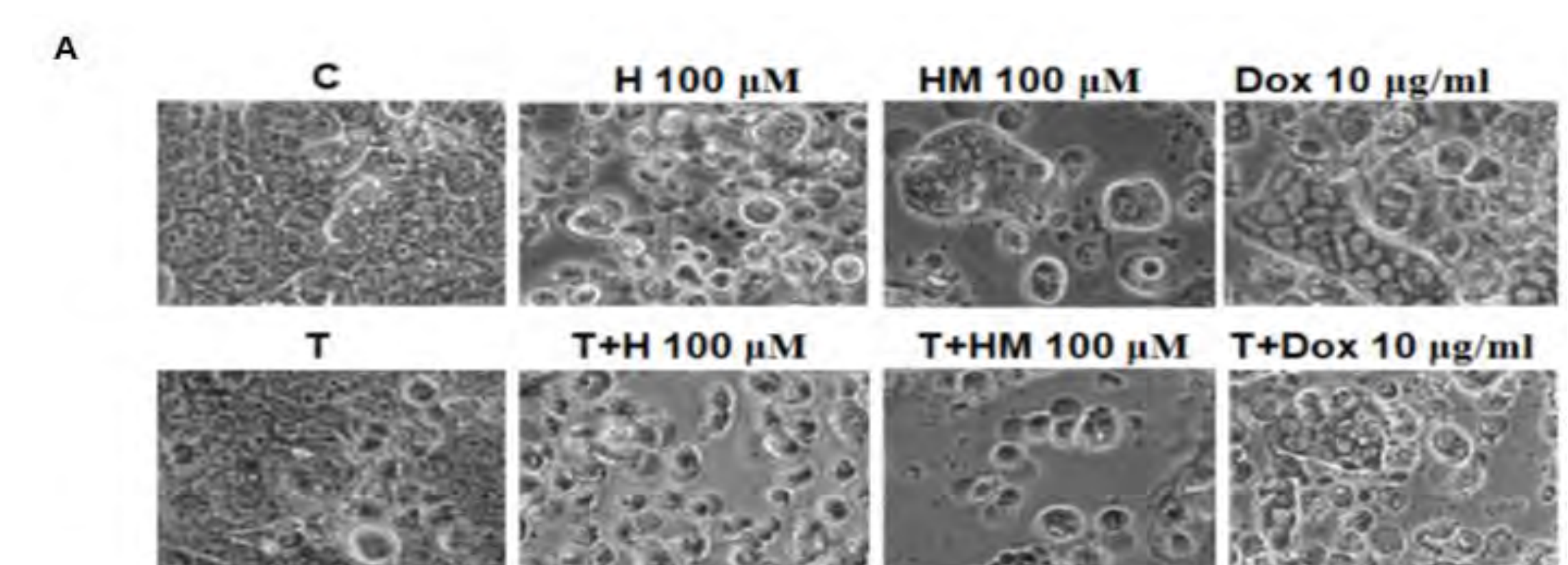
Here, 7-methoxyheptaphylline enhanced TRAIL-induced cleavage of caspase-3 in HT29 cells.



Effect of 7-methoxyheptaphylline on DR5 mRNA expression in HT29 cells. The result from RT-PCR (A) and real-time RT-PCR (B). n=3, ^a p < 0.05, ^{aa} p < 0.01.



Effect of 7-methoxyheptaphylline on HT29 cells and TRAIL-induced HT29 cells. n=3, ^a p < 0.01, ^{aa} p < 0.001, ^a comparing between cells treated with 7-methoxyheptaphylline and control, ^b comparing between cells treated with 7-methoxyheptaphylline combined with TRAIL.



Activity of heptaphylline and 7-methoxyheptaphylline on HT29 cells and TRAIL-induced HT29 cells. Cell morphology observed by phase contrast microscopy (A) and cell viability from MTT assay. C: control, T: TRAIL 200 ng/ml, H: heptaphylline, HM: 7-methoxyheptaphylline, Dox: doxorubicin. n=3, ^a p < 0.05, ^{aa} p < 0.01, ^a comparing between cells treated with compounds and control, ^b comparing between cells treated with compound alone and combined with TRAIL.

References

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Acknowledgement



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