Screening of Urea Transporters Inhibitors in *Apium graveolens* seeds by UPLC-TOF-MS

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Background

Urea transporters (UTs), which are membrane channel proteins, facilitate urea transmembrane permeability and play an important role in urine concentration mechanisms. Several UT knockout mouse models showed that UT deletion caused polyuria and did not result in electrolyte imbalance[1]. These results indicate that UTs are a superior diuretic target. The *Apium graveolens* L. seeds are rich in carbohydrates and protein, which are stomachic, diuretic, blood purifier, menstrual regulator, hypotensive, and sedative.

Objective

This study was designed to find small molecules with UT-B inhibitory activity in natural products- celery seeds.

Methodology

- **Analysis of celery seed extracts:** Analyses were carried out using an ACQUITY Ultra Performance LC system equipped with a mass detector TOF mass spectrometer and an electrospray ionization (ESI) source.
- **ADMET prediction and molecular docking:** The active compounds, extracted from celery seeds, were obtained by using Discovery Studio and the ADMET property prediction.
- **Inhibitory activity:** The inhibitory activity of compounds was assayed by using erythrocyte lysis assays[2]. Configure 1% red blood cell suspension (RBCs), which contains 1.25 M acetamide and 5 mM glucose. The assayed compounds were prepared in two concentrations of 25 μM and 100 μM, and phloretin as a positive drug was used as a control. A vessel containing 99 μL of the suspension of RBCs was added with 1 μL of the assayed compound, incubated for 20 min and then 20 μL was added to the isotonic buffer. The absorbance value was measured at 410 nm using a microplate reader. The $\%lysis=100\%*(A_{neg}-A_{test})/(A_{neg}-A_{pos})$, where A_{test} is the absorbance value from a test well.

Results

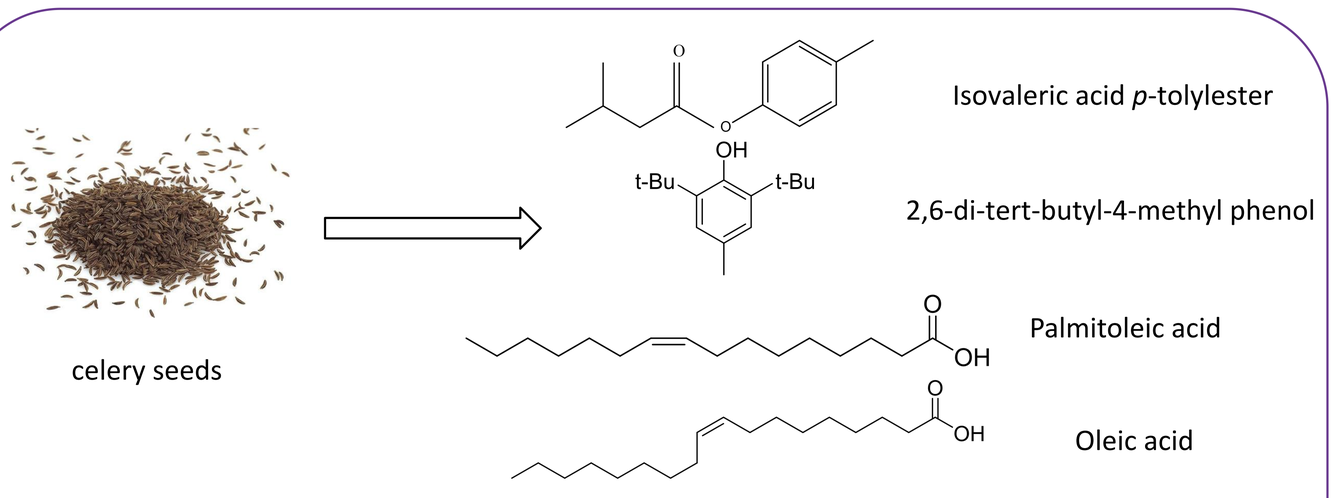

Fig.1 The structures of active compounds extracted from celery seed

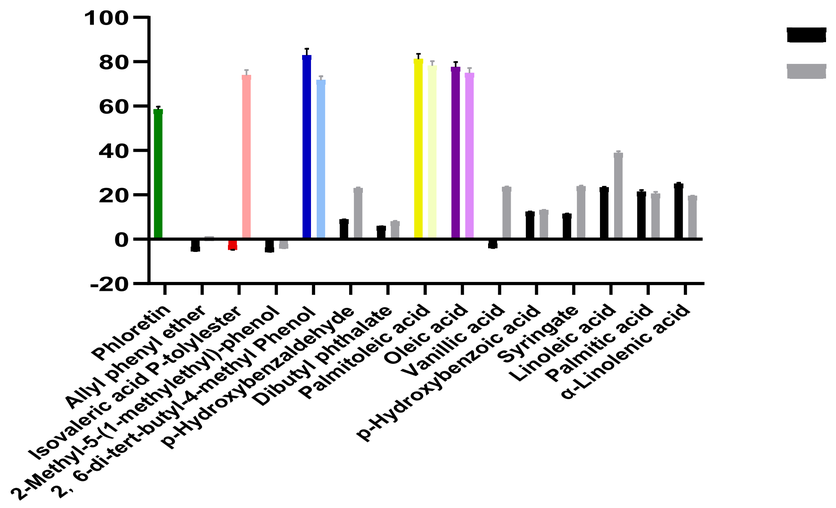

Fig.2 The inhibition rate of compounds extracted from celery seeds. (The positive drug was marked with green; The active compounds were marked with pink, blue, yellow, and purple)

Conclusion

These findings suggest that the discovery of UT-B inhibitors in natural products is possible and contributes to the development of novel diuretics.

References

1. Yang, B., et al., *Urea-selective concentrating defect in transgenic mice lacking urea transporter UT-B.* J Biol Chem, 2002. **277**(12): p. 10633-7.
2. Levin, M.H., R. de la Fuente, and A.S. Verkman, *Urearetics: a small molecule screen yields nanomolar potency inhibitors of urea transporter UT-B.* FASEB J, 2007. **21**(2): p. 551-63.

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