Novel natural products LP-01 and LP-02 demonstrated in vitro and in vivo antitumor and chemopreventive activity but their mechanism of action is not well known. In this study, we investigated the effects of LP-01 and LP-02 on serum kallikreins by western blot and on proteomic patterns assessed by SELDI-TOF mass spectrometry. Murine sera were obtained from human lung carcinoma xenografts A549, MV-522 and SK-MES treated with LP-01 and LP-02 (500 and 4000 mg/kg doses) and the vehicle group (10% DMSO). Western blots and on proteomic patterns assessed by SELDI-TOF mass spectrometry. Murine sera were obtained from human lung trials conducted in patients at high risk of lung cancer, we evaluated the effects of LP-01 and LP-02 on serum kallikreins by western blot and on proteomic patterns assessed by SELDI-TOF mass spectrometry. Murine sera were obtained from human lung carcinoma xenografts A549, MV-522 and SK-MES treated with LP-01 and LP-02 (500 and 4000 mg/kg doses) and the vehicle group (10% DMSO).

**METHODS**

(+) control

groups. SELDI analysis provided early insight into model- and treatment-specific clusters mainly in the range of 4,000 to 20,000 mass-antibodies with different kallikrein specificity. Multiple bands of 86-40 kD were observed, consistent with a known heterogeneity of carcinoma xenografts A549, MV-522 and SK-MES treated with LP-01 and LP-02 (500 and 4000 mg/kg doses) and the vehicle given as pretreatment and sacrifice groups in the 14,000 to 17,000 (M/Z) range. The results warrant further investigation of the serum proteins to-charge (M/Z) ratios, which might be associated with drug response. Cluster analysis revealed large differences among experiment (sacrifice).

**RESULTS**

- Mice were treated with LP-01, and LP-02 (500 and 4000 mg/kg doses) and the vehicle given p.o., qd to end with 1-3 rounds of drug pretreatment prior to implantation of human lung carcinoma xenografts A549, MV-522 and SK-MES. Serum proteins were resolved by SDS PAGE, transblotted to Hybond-C membranes and incubated with anti-kallikrein antibodies with enhanced chemiluminescence detection.

**CONCLUSIONS**

- Multiple protein bands were detected with kallikrein antibodies.
- The patterns of proteins cross-reactive with kallikrein antibodies showed differences between antibodies and models, and the treatment groups.
- SELDI analysis demonstrated time- and dose-dependent effects of LP-01 and LP-02 on serum protein patterns.
- Members of serum kallikrein family could represent potential biomarkers of LP-01 and LP-02 efficacy in clinical trials with the drugs.
- SELDI serum profiling is a feasible approach to investigating surrogate endpoints of LP-01 and LP-02 efficacy in the clinic.

**SUMMARY**

- Results warrant further investigation of the serum proteins to-charge (M/Z) ratios, which might be associated with drug response. Cluster analysis revealed large differences among pretreatment and sacrifice groups in the 14,000 to 17,000 (M/Z) range. The results warrant further investigation of the secreted proteins and their potential role in the pathology and clinical outcome of human lung cancer xenograft models.

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