SUMMARY OF DISSERTATION

Name of Doctoral candidate: Bui Thi Xuan

Dissertation title: "Study on chemical constituents and toxicity and biological effects to support the treatment of gastric, duodenal ulcers of *Sanchezia nobilis* Hook.f."

Specialty: Medicinal Materials - Traditional Pharmacy

Code of specciality: 9720206

Name of academic advisors:

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2. Dr. Tran Thanh Ha

Name of the academic institute: National Institute of Medicinal Materials

Summary of the dissertation

1. Objectives

- To isolate pure compounds from the extract and identify their chemical structure.
- To evaluate the toxicity, anti-inflammatory effects of peptic ulcers, and central pain relief of total and fractional extracts.

2. Methods

2.1. Botanical study

- Scientific name identification: Morphological characteristics were in comparison with the standard specimens of *Sanchezia nobilis* Hook.f.

2.2. Chemical study

- Extraction and isolation of chemical constituents:

The research sample collected in Co Le commune, Truc Ninh district, Nam Dinh province was washed, chopped, and dried at 50-60^{o}C, then ground into a coarse powder, and extracted by different methods to get the extract. Total extract and fractional extracts were used to evaluate anti-gastric ulcers in a pyloric ligation model in white rats. The obtained results are the basis for selecting extraction fractions and isolating compounds, specifically as follows:

+ Isolation of compounds from the *n*-hexane fraction by normal phase column chromatography. Fractions during isolation were monitored by thin-layer chromatography.

+ Isolation of compounds from ethyl acetate fraction: Extraction of the alkaloid-rich segment was carried out with tartric acid (2%) and the residue left after extraction of alkaloids was extracted with ethyl acetate. Alkaloid-rich segment isolated compounds by normal phase column chromatography. The remaining ethyl acetate fraction was isolated by normal phase column chromatography, reversed phase, sephadex, and prepared liquid chromatography. Fractions during isolation were monitored by thin-layer chromatography.

- Structural elucidation of isolated compounds: Chemical structures were identified based on their physical properties (melting points, rotary polarization) and spectroscopy analysis: FT-IR, UV-Vis, ESI-MS, HR-EI-MS 1D-NMR, 2D-NMR, and in comparison with the published data.

2.3. Biological study

- Evaluation of acute toxicity of the total extract and extract fractions of dried leaves of *Sanchezia nobilis* Hook.f. according to the Ministry of Health, WHO.

- Evaluation of sub-chronic toxicity according to OECD guidelines for the testing of chemicals.

- Evaluation of the anti-inflammatory effect of gastric ulcer on the pyloric ligation model in white rats (Shay).

- Evaluation of the central analgesic effect on the hot plate model and pain threshold meter.

3. Results and Conclusion

3.1. Botanical properties

- Scientific name of the sample collected in Co Le Commune, Truc Ninh District, Nam Dinh Province was identified as *Sanchezia nobilis* Hook.f. (Acanthaceae)

3.2. Chemical constituents

The structure of 20 compounds isolated from *n*-hexane, ethyl acetate of leaves of *Sanchezia nobilis* Hook.f. were identified as followings: 12 flavonoids (hispidulin,

kaempferol, afzelin, hispidulin-7-*O*-*β*-glucopyranoside, hispidulin-4′-*O*-*β*-glucopyranoside, hispidulin-7-*O*-*β*-glucuronide methyl ester, hispidulin-7-*O*-*β*-glucuronide, apigenin, apigenin-7-*O*-*β*-glucuronopyranosid, quercetin, hyperosid, and rutin); 3 sterol derivatives (*α*-spinasterol, stigmast-4-ene-3,6-dion, and daucosterol); 2 alkaloid ((+)-13-*O*-acetylfawcettimine and (+)-fawcettidine); 2 triterpenoid (acid coccinic and acid betulinic) and 1 coumarin derivatives (7-hydroxy-6-methoxy coumarin). In which:

+ 1 new compund was (+)-13-*O*-acetylfawcettimine.

+ 13 compounds were isolated from genus *Sanchezia* for the first time: *α*-spinasterol, stigmast-4-ene-3,6-dion, 7-hydroxy-6-methoxy coumarin, acid coccinic, acid betulinic, (+)-fawcettidine, hispidulin, kaempferol, afzelin, hispidulin-7-*O*-*β*-glucopyranoside, hispidulin-4′-*O*-*β*-glucopyranoside, hispidulin-7-*O*-*β*-glucuronopyranosid methyl ester, and hispidulin-7-*O*-*β*-glucuronopyranoside.

3.3. Toxicity and Biological activities

- Acute toxicity: The LD50 dose of the total extract and the fractions of the leaf extract has not been determined at the test dose level of 12g/kg body weight of mice.

- Sub-chronic toxicity: At doses of 50 and 250 mg/kg rat body weight/day of the ethyl acetate fraction, no sub-chronic toxicity was observed in rats after 28 days of continuous administration.

- Anti-inflammatory effect on stomach ulcers:

+ Total extract (50 mg/kg/day) has not shown an anti-ulcer effect in the pyloric ligation model in white rats through its effect on reducing ulcer score, the severity of ulcer damage, decrease in gastric volume and gastric pH.

+ Total extract (150 and 450 mg/kg/day) was effective in reducing gastric ulcers in the pyloric ligation model in white rats.

+ Fraction *n*-hexane and ethyl acetate (50 mg/kg/day) have the effect of reducing gastric ulcer in the pyloric ligation model in white rats through the effect of reducing ulcer score, the severity of lesions, ulceration, total acidity, and gastric pH.

+ Water fraction (100 mg/kg/day) has not shown an anti-ulcer effect.

- Regarding pain relief:

+ Total extract doses of 300 and 900 mg/kg/day, water fractions doses of 200 and 600 mg/kg/day, and ethyl acetate fractions doses of 100 mg/kg/day (equivalent to ulcer reduction dose in mice) have not shown a central analgesic effect.

+ Fractions of *n*-hexane (100 and 300 mg/kg/day) and high dose of ethyl acetate at a dose of 300 mg/kg/day had shown central analgesic effects in white mice.

Ha Noi, December 2022

ACADEMIC ADVISORS **DOCTORAL CANDIDATE**

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