Analyte	Concentration (ng/ml)	Accuracy (% recovery) *Requirement: 80 - 110%*	Precision	
			Intraday (Max value of RSD (%)	***Interday*** (Max value of RSD (%)
LOR	1	81.6 - 109.1	9.07	9.03
	5	89.1 - 105.3	5.56	5.40
	20	82.2 - 108.1	6.08	10.5
	50	91.4 - 107.7	4.92	5.21
PRO	1	80.3 - 109.1	8.91	9.15
	5	81.8 - 108.1	6.82	9.27
	20	82.9 - 108.2	7.07	5.45
	50	88.1 - 108.2	5.16	6.60

Requirement for intraday and interday precision:

- RSD is not more than 15% and 22%, respectively, at concentration of 1 ppb (100 ppb calculated on matrix);

- RSD is not more than 11% and 16%, respectively, at concentration of 5 (500 ppb calculated on matrix);

- RSD is not more than 7.3% and 11%, respectively, at concentration of 20 and 50 ppb (1.25 ppm and 5 ppm calculated on matrix).

3.3.3. Applications:

Applying the developed method and analyzing over 35 samples of herbal preparations and products used to treat or support the treatment of colds, flu, urticaria, allergies... Samples include 25 solid samples (pills, capsules, powders, tablets, tea bags) and 10 liquid samples (solution, liquid suspension) for oral use and nasal spray. The results showed that 6 samples were positive for the targeted analytes, are presented in Table 4 and illustrated in Fig. 2.

Table 4. Analysis results of positive samples

No.	Code	Formulations	Content (mg/ g)				
			CIN	CLOR	CYP	LOR	PRO
1	BNH93CU	Powder	-	1.390	-	-	-
2	HA29	Soft pills	0.048	0.658	-	-	-
3	HCH99	Hard pills	-	0.596	-	-	-
4	VNA02	Capsule	-	0.984	0.329	0.096	-
5	VNA05	Capsule	-	1.340	-	-	-
6	VNA35	Capsule	-	3.131	0.730	-	-

"-": < LOD.

In general, illegal addition of H1 antihistamines into herbal preparations not only occurs in Vietnam [5,6] but also in other countries, especially in Asia where herbs are commonly used to prevent and treat diseases [7, 8]. In the previous study [6], we developed a LC-MS/MS method to analyze three H1-antihistamines, namely LOR, CYP, CLOR in solid drug samples. This study has built a method to analyze all five H1 antihistamines in the control list of the Ministry of Health [4] and expanded to include liquid samples, hence, it will cover a broader sample population.

Among 35 samples of herbal preparations used for treatment and support for the treatment of allergies, urticaria, itching, and flu, 6 samples were found to be positive for target substances. Especially, CLOR was detected in all postive samples. This can be explained by the effect of this drug, as well as the familiarity and low cost of CLOR. In particular, there was 1 sample that was positive for 3 substances CLOR, LOR, CYP at low levels, which would cause difficulties in the quality inspection and assessment. All of these positive samples do not have registration/publication numbers and are purchased online or sent by suspicious users. Therefore, users need to consider the source of supply when purchasing herbal products.

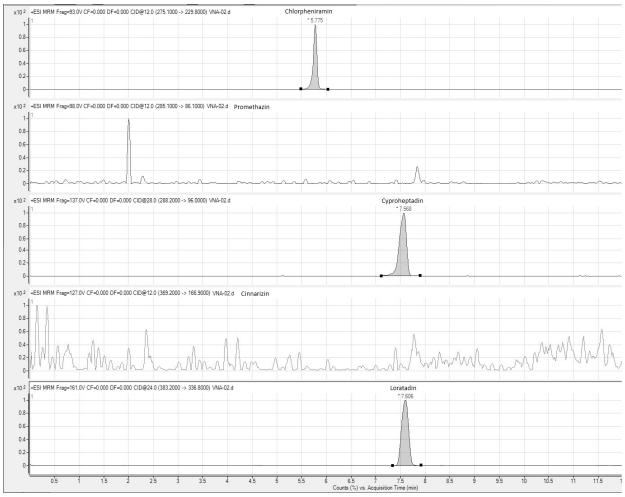

Fig. 2. Chromatogram of VNA02

4. Conclusion

The study has developed an LC-MS/MS method to simultaneously identify cinarizine, promethazine, chlorpheniramine, cyproheptadine,

and loratadine illegally mixed in herbal preparations. Sample treatment is quick and simple. The analytical method has high specificity, low detection limit, accuracy and precision met the requirements of AOAC 2016. The method has high feasibility in analyzing real samples circulating in the market. The study analyzed and found 17.1% positive samples (6 out of 35 tested samples), detected 4 out of 5 research active pharmaceutical ingredients adulterated in the samples, except promethazine, with concentrations ranging from 0.048 to 3.13 mg/g.

Acknowledgment: This study was supported by Ministry of Health, project titled *« Developing a method for simultaneous analysis of drugs in antihistamine and antihypertensive groups illegally mixed in traditional herbal preparations by HPTLC, HPLC and LC-MS/MS »* period 2021 - 2023.

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Journal of Medicinal Materials, 2023, Vol. 28, No. 3 (pp. 177 - 184)

ANTI-INFLAMMATORY EFFECTS OF CHROMONES AND SESQUITERPENOIDS FROM THE AGARWOOD OF *AQUILARIA CRASSNA*

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(Received May 24th, 2023)

Summary

Anti-Inflammatory Effects of Chromones and Sesquiterpenoids from the Agarwood of *Aquilaria crassna*

Aquilaria crassna Pierre ex Lecomte is the most dominant species of the genus *Aquilaria*, which is widely distributed from the south to the north of Vietnam. In Vietnam, agarwood from *A. crassna* has been used in traditional medicine to treat insomnia, anxiety, asthma, pain, and digestive disorders. Our continuous research on the agarwood from *A. crassna* led to the isolation of fourteen compounds, which were identified as 12-hydroxy-4(5),11(13)-eudesmadien-15-al (**1**), 4'-methoxy-2-(2-phenylethyl)chromone (**2**), baimuxinic acid (**3**), 1-hydroxy-1,5-diphenylpentan-3-one (**4**), 5-hydroxy-7,4'-dimethoxyflavone (**5**), 6,7,4'-trimethoxy-2-(2-phenylethyl)chromone (**6**), 6,4'-dimethoxy-3'-hydroxy-2-(2-phenylethyl)chromone (**7**), 6,3'-dimethoxy-4'-hydroxy-2-(2-phenylethyl)chromone (**8**), 6-methoxy-4'-hydroxy-2-(2-phenylethyl)chromone (**9**), 4'-hydroxy-2-(2-phenylethyl)chromone (**10**) 6-methoxy-2-(phenylethyl)chromone (**11**), 5-hydroxy-6,4′-dimethoxy-2-(phenylethyl)chromone (**12**), 6-hydroxy-2-(2-phenylethyl)chromone (**13**), 6-hydroxy-2-[2-(4'-methoxyphenyl)ethyl]chromone (**14**), from the ethyl acetate fraction of agarwood of *A. crassna*. Their structures were determined by means of spectroscopic methods (MS, 1D, and 2D-NMR). The anti-inflammatory effects of extracts and isolated compounds were evaluated against NO production in microglial BV2 cells.

Keywords: *Aquilaria crassna*, *Anti-inflammatory effects, Agarwood, Chromone, Sesquiterpenoid.*

1. Introduction

Agarwood is a fragrant resin produced inside the heartwood of various *Aquilaria* species when injured by insects, physical cuts, microbial infections, or chemical stimulation. In recent studies, sesquiterpenoids and chromone derivatives from agarwood were reported to have anti-neuroinflammatory, antibacterial, α-glucosidase inhibitory, cytotoxic, acetylcholinesterase inhibitory, neuroprotective, and antidepressant activities. *Aquilaria crassna* (Thymelaeaceae) produced a popular type of agarwood, which was found in the rainforests of the Indo-Malesia region [1],[2]. It has also been