**Green and Scalable Semi-Synthesis of Pharmaceutical-Grade Quercetin from** ***Styphnolobium japonicum* (L.) Schott**

**Anh Vu Nguyen1**, Ngan Ha Nguyen2, Phuong Lan Le3, Ngoc Phuc An Le4, Khanh Linh Trinh5, Nam Phong Nguyen6, Thi Hien Pham7, Van Hai Nguyen7.

Faculty of Basic Science, Hanoi University of Pharmacy1, Hanoi, Vietnam;

Lycée Français Alexandre Yersin2, Hanoi, Vietnam;

High School for Gifted Students, Hanoi National University of Education3, Hanoi, Vietnam;

Nguyen Tat Thanh School, Hanoi National University of Education4, Hanoi, Vietnam;

Vinschool The Harmony5, Hanoi, Vietnam;

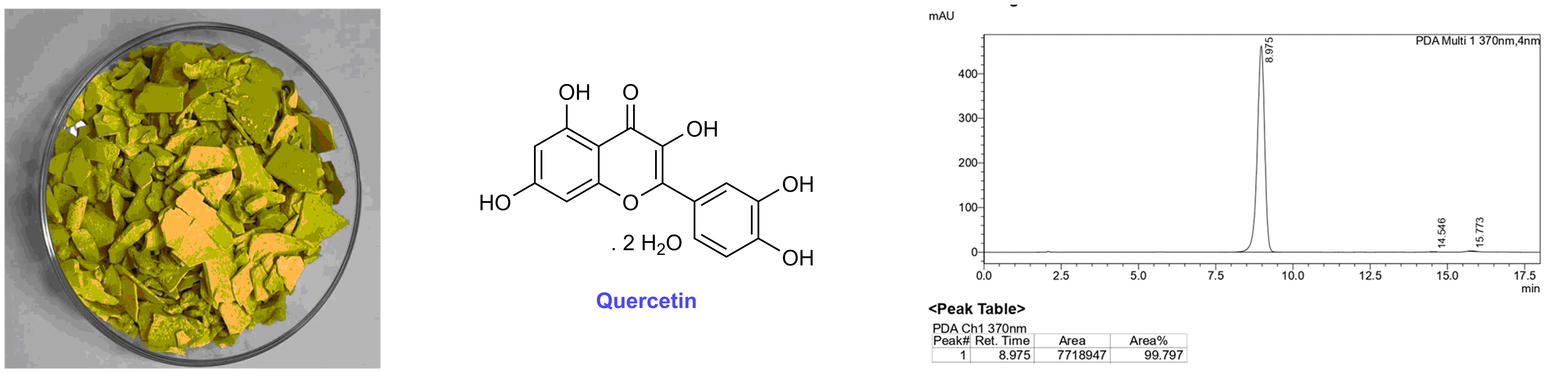
Tran Phu High School - Hoan Kiem6, Hanoi, Vietnam;

Faculty of Pharmaceutical Chemistry and Technology, Hanoi University of Pharmacy7, Hanoi, Vietnam.

**Background and aims.** Researchers from all around the world have been very interested in quercetin because of its many biological activities and promising pharmaceutical benefits. Traditional techniques of extraction and semi-synthesis via rutin hydrolysis for obtaining pharmaceutical-grade quercetin frequently involve multi-step purification and hazardous solvents, which restricts their scalability and sustainability. In this study, we developed a scalable, environmentally friendly semi-synthesis method to produce quercetin that satisfies pharmacopoeial standards utilizing rutin from *Styphnolobium japonicum*, a sustainable source that is widespread in Vietnam and other countries.

**Methods.** Using a 2% borate solution, rutin (95% purity) was extracted from *Styphnolobium japonicum* (L.) Schott (dried flower buds). Rutin was hydrolyzed to produce quercetin, and TLC was used to monitor the reaction's development. Quercetin quality was assessed using the specifications described in the USP 44 – NF 39 monograph, and HPLC measurement was confirmed in compliance with ICH guidelines. Using spectroscopic methods such as ¹H-NMR and ¹³C-NMR, IR and MS, the structure of quercetin was verified.

**Results.** At a batch size of 10.0 g, the hydrolysis of rutin was conducted at 80 to 90°C for two hours using a reaction media consisting of a 3:1 ratio of 96% ethanol to 20% HCl. A variety of solvents, such as isopropanol, ethanol, dichloromethane, and water (with pH modification), were used to investigate the purification of the crude product. A pharmacopeia-grade purification method was successfully developed, consisting of the following two stages: (*i*) Fractional precipitation at pH 4.0 produced a product with 99.8% purity and 0.3% total impurities, satisfying the requirements of the applicable pharmacopeial monograph; (*ii*) recrystallization in 96% ethanol at a solvent-to-solid ratio of 30:1 (v/w).



**Figure 1.** The obtained quercetin and its HPLC chromatogram.

**Conclusion/Discussion.** We successfully developed a semi-synthetic method for producing pharmacopeia-grade quercetin from rutin, achieving a yield of 47%. Adjusting the pH in an aqueous medium and then recrystallizing in 96% ethanol is a unique and unpublished purification technique. This technique enables the use of safe solvents and reagents, great scalability, and a readily available and sustainable natural feedstock, *Styphnolobium japonicum*.

**References:**

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