VUB GENEESKUNDE & FARMACIE

جامعة عمار ثليجي الأغواط
Université Amar Telidji - Laghouat

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INVITATION to the Public defence of

Ziyad Ben AHMED

To obtain the academic degree of

'DOCTOR OF PHARMACEUTICAL SCIENCES-VUB'
'DOCTOR OF SCIENCES
– SPECIALTY: CHEMISTRY-U. AMAR TELIDJI'

Phytochemical analysis and simultaneous determination of the in-vitro antiradical, antidiabetic and antihypertensive activities of Pistacia atlantica leaf extracts

The public defence will take place on

Wednesday, **18 December 2024 at 4:30 p.m.**

In Auditorium Piet Brouwer
VUB Health Campus
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussels

and can be followed online, accessible through the following link:
https://gf.vub.ac.be/redirects/PhD_defense_Ziyad_Ben_Ahmed.php

Summary of the dissertation

This research investigates *Pistacia atlantica* Desf., an underexplored plant in Algeria, for its potential as a source of bioactive compounds with antioxidant and pharmacological properties. With the growing global interest in herbal medicines due to their health benefits and cost-effectiveness, there is an urgent need for accurate identification and standardized production of these products. The complex chemical composition of herbal products presents challenges for their analysis, emphasizing the need for reliable methods, such as fingerprinting, for quality control and active ingredient identification. The study focuses, in a first instance, on optimizing the extraction of phenolic compounds from *P. atlantica* leaves using an experimental design approach. Key factors, as extraction time, temperature, and liquid-to-solid ratio, were evaluated, with the latter found to be the most influential on extraction efficiency. The study also explores how harvest period, growing region, and gender affect the phenolic, flavonoid, and tannin contents, as well as the antioxidant activities. Seasonal variations show that spring is the optimal time for leaf collection, as it results in higher total phenolic content and antioxidant capacity. To measure antioxidant activity, various methods were employed, i.e. spectrophotometric assays based on hydrogen atom transfer or single-electron transfer. An acetone-water crude extract was analyzed for its antioxidant properties using seven free radical assays, which were grouped into non-biological and biological radical producers. Three assays using stable, non-biological radicals, and four using biological radicals provided insights into the extract's protective action. The study also utilized chromatographic and chemometric approaches for the identification of active compounds. The antioxidant activities were modeled using partial least squares regression based on HPLC fingerprints. Considering these models, using three assays was recommended to evaluate the global overall antioxidant capacity of *P. atlantica* leaves. Furthermore, chromatographic fingerprinting combined with multivariate calibration was used to investigate the enzyme inhibitory effects of *P. atlantica* leaves on α-amylase, α-glucosidase, and angiotensin I-converting enzyme. Thirteen compounds were identified as responsible for these activities, with digalloylquinic acid demonstrating significant inhibitory effects on both α-amylase and α-glucosidase, surpassing the known inhibitor acarbose. Furthermore, a novel approach combining molecular docking with chromatographic fingerprinting was utilized to efficiently identify potential bioactive compounds from an acetone-water crude extract. This *in silico* method predicts the interactions between phytochemicals and target enzymes, such as α-amylase and α-glucosidase, which are important in managing hyperglycemia in type 2 diabetes. The findings confirm that digalloylquinic acid has a strong binding affinity to the target enzymes and indicate no toxic effects. These results suggest that *P. atlantica* may have promising potential for managing type 2 diabetes, with further *in vivo* studies needed to validate these therapeutic effects.

Curriculum Vitae

Ziyad Ben Ahmed was born on November 24, 1980, in Algeria. He obtained a Baccalaureate in Experimental Sciences in 1998 at the Imam El Gazahli School in Laghouat. He earned his State Engineer diploma in Industrial Chemistry, specializing in Organic Process Engineering, in 2004 at the Faculty of Technology, Amar Telidi University, Laghouat. He then completed his Magister degree in Chemistry in 2009, specializing in Natural Products Chemistry, at the Faculty of Science, Zian Achour University, Djelfa, with a research subject titled "The Fruit of Atlas Pistachio: Fatty Acid Composition, Tocopherols, and Antioxidant Activity."

In 2010, Ziyad began his PhD at the Laboratory of Fundamental Sciences, Amar Telidji University, Laghouat, Algeria, under the supervision of Prof. M. Yousfi. In 2013, a joint PhD with the Department of Analytical Chemistry, Applied Chemometrics, and Molecular Modelling at Vrije Universiteit Brussel, Belgium, was started under the supervision of Prof. Y. Vander Heyden. During his PhD, Ziyad spent 18 months at Vrije Universiteit Brussel, focusing on "Phytochemical analysis and simultaneous determination of the in-vitro antiradical, antidiabetic, and antihypertensive activities of *Pistacia atlantica* leaf extracts." Throughout his PhD, he published 11 papers as first author in peer-reviewed international journals, and one book chapter, with additional papers in preparation. He is also co-author of five other published papers. He also participated in congresses, scientific days, seminars, and workshops, presenting both poster and oral presentations. Additionally, Ziyad served as the co-promoter for 14 master's theses and assisted in courses, such as Strategies and Tools in Organic Synthesis and Organic Chemistry, for the Master's program in Natural Products Chemistry at the Faculty of Science, Amar Telidi University, Laghouat.