UNIVERSITATEA BABEȘ-BOLYAI

Faculty of Physics

Doctoral School of Physics

PhD Thesis Summary

Developing Innovative Applications of Biogenic Carbonates Assisted by Raman Technology and Complementary Methods in Line with the Bioeconomy Concepts

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Abstract

In response to the global imperative of transitioning toward a circular bioeconomy, this thesis explores the valorization of biogenic waste materials into high-value applications spanning pharmacology, biomedicine, and environmental engineering. By utilizing low-cost, renewable biological resources—primarily composed of waste-derived calcium carbonates—this research presents sustainable, scalable, and cost-effective alternatives to conventional material production methods. Central to the study is the application of Raman Spectroscopy, which offers rapid, non-invasive, and highly sensitive characterization of complex organic-mineral matrices. Complementary techniques, including X-ray Diffraction (XRD), Scanning Electron Microscopy (SEM), and Infrared Spectroscopy (IR), further support material analysis and validation.

Structured into three chapters, the thesis first investigates the composition and morphology of calcium carbonate-based biomaterials, highlighting the power of Raman technology in elucidating their intricate structures. The second chapter advances this foundation by developing novel pharmaceutical formulations and drug carriers derived from biogenic precursors. The final chapter demonstrates the conversion of waste crab shell-derived Mg-calcite into calcium phosphate minerals, underscoring Raman Spectroscopy's role in monitoring and controlling this transformation.

The findings emphasize the dual impact of this research: the development of functional, application-ready bio-based materials and the broader contribution to environmental and economic sustainability through waste reduction and material circularity. This work not only illustrates the practicality of using Raman Spectroscopy in bioresource valorization but also lays a foundation for future innovations in sustainable material science and biotechnology. The results presented were published in the form of 7 research articles (3 Q1; 3 Q2; 1 N/A), included in the thesis, with the total AIS = 4.713

Table of Contents

Introduction

The current global push for a sustainable and resource-efficient economy has gained significant momentum, driven by the urgent need to mitigate environmental degradation and optimize resource utilization. At the heart of this transition lies the concept of the bioeconomy, which promotes the use of renewable biological resources for the production of bio-based products, energy, and services. A critical aspect of this framework is the valorization of biogenic materials, particularly biogenic waste, to ensure sustainability and reduce environmental impact. Among the many analytical techniques employed in the study and transformation of biogenic materials, Raman spectroscopy has emerged as a highly effective tool, as it can be seen from the growing trend in the number of articles published in the last 15 years (meta-analysis Figure 1.1).

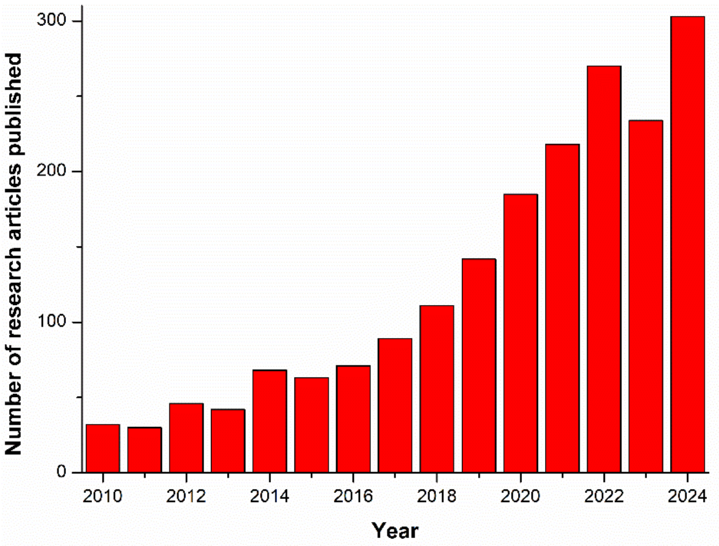


Figure 1.1 Number of research articles published in the last 15 years according to Science Direct database (Accessed April 3, 2025), when using the search keywords: Raman Spectroscopy' and 'biogenic materials'.

This non-destructive and highly sensitive spectroscopic technique allows for rapid, in-situ analysis of molecular structures, offering invaluable insights into the composition, chemical interactions, and potential applications of bio-based resources. Its versatility spans multiple disciplines, including material science, pharmaceuticals, food technology, and environmental monitoring, thereby facilitating the development of innovative and sustainable solutions. One of the key advantages of current Raman technology is its ability to generate highly specific molecular fingerprints, simultaneously addressing sboth organic and inorganic counterpart, without requiring extensive sample preparation, making it indispensable tool for both scientific research and industrial applications.

In the realm of biogenic material valorization, Raman spectroscopy plays a pivotal role in identifying key structural components, monitoring chemical modifications, and assessing the quality of bio-based products.

Although Sir C.V. Raman characterized himself for the first time a biogenic material (pearls from mussels) and published his findings in the Proc. of Indian Academy of Science in 1935, quoting "*The present investigation indicates that the subject has so far been only very imperfectly explored and offers much scope for further research*" [C. V. Raman, 1935, https://www.ias.ac.in/article/fulltext/seca/001/09/0567-0573] and that was in the time of not yet discovered lasers, the current technology with improved detection speed, sensitivity, resolution and flexibility, along with multiple laser lines availability, allows unprecedent capability in materials characterization and processes monitoring. The development of portable Raman spectrometers has further broadened its applications, enabling real-time, on-site analysis, which is particularly advantageous for process monitoring. The available portable Raman devices provide rapid, non-invasive measurements of raw materials, intermediate products, and final bio-based goods, eliminating the need for complex laboratory infrastructure. Additionally, surface-enhanced Raman scattering (SERS) significantly increased the detection sensitivity, enabling the identification of low-concentration analytes that would otherwise be undetectable through conventional Raman techniques. In the context of biogenic material valorization, SERS proves particularly useful for detecting minor biochemical components, optimizing bioprocesses, and ensuring the quality and functionality of bio-based products. One class of biogenic materials that holds substantial scientific and industrial relevance is calcium carbonate ($CaCO_3$)-based compounds. These materials, which are found in marine organisms (such as mollusk shells, coral reefs, and crustacean exoskeletons) and terrestrial sources (such as eggshells), exhibit unique physicochemical properties that make them valuable for applications in biomedicine, material science, and environmental engineering. However, a considerable proportion of calcium carbonate-based biogenic materials exists as waste, particularly from industries like food processing, aquaculture, and construction. The improper disposal of these materials contributes to environmental pollution and inefficient resource use, emphasizing the need for innovative valorization strategies. Biogenic calcium carbonate is particularly attractive for biomedical applications due to its biocompatibility and the ease with which it can be modified at the nanoscale. Research efforts are being focused on exploring its potential in drug delivery systems, particularly in cancer therapy, where its dissolution in acidic environments (such as tumor sites) can be exploited for targeted release of therapeutic agents. Additionally, it is being investigated for bone regeneration applications, as it can promote mineralization and support new bone tissue growth. Biogenic $CaCO_3$, derived from natural sources such as marine organisms, plants, and certain microorganisms, offers distinct advantages over synthetic materials, including lower toxicity, straightforward synthesis methods, and cost-effectiveness due to its abundance in waste streams. However, several challenges remain before its widespread industrial implementation, including stability in physiological conditions, optimization of drug loading efficiency, and the scalability of manufacturing processes. Raman spectroscopy is instrumental in characterizing and processing calcium carbonate-based waste materials by providing detailed insights into their chemical composition and structural properties. It also aids in monitoring and refining processing methods for converting waste into high-value products.

Aim and scope of the thesis

Given the global urgency surrounding the valorization of biogenic resources, the work presented in this thesis represents a concerted effort to address this critical issue, with the aim of developing high-value applications out of otherwise wasted materials. The research undertaken explores innovative ways to repurpose biological waste into useful products, spanning multiple scientific and industrial domains, including pharmacology, biomedicine, and environmental engineering. The key advantages of the developed applications lie in their simplicity, accessibility, and cost-effectiveness. Unlike conventional methods that may require complex processes and expensive raw materials, the approaches employed in this research prioritize the utilization of low-cost, abundant, and renewable biogenic waste. Because the base materials used in thie studies are primarily derived from waste streams, their large-scale industrial implementation would present minimal logistical or economic challenges. Furthermore, the treatment and processing methodologies employed are designed to be straightforward, reproducible, and easily scalable. The experimental procedures rely on minimal energy-intensive steps, ensuring sustainability and feasibility in industrial applications. The materials developed can be produced using simple instruments such as mechanical grinders or ball mills, while the chemical reagents required—sodium hydroxide, hydrochloric acid, or phosphoric acid—are inexpensive and widely accessible. This focus on simplicity and resource efficiency underscores the potential of these methods to be widely adopted in both high-tech research environments and resource-constrained settings.

The significance of this research is twofold. Firstly, it provides tangible, high-value novel products with diverse applications, such as drug formulations, bone replacement materials, and biostimulants or fertilizers for soil amendments. Secondly, it contributes to broader environmental and economic sustainability by mitigating waste accumulation and promoting a circular bioeconomy. By repurposing biological waste into functional nanomaterials, this work not only aligns with global sustainability goals but also presents viable alternatives to traditional, resource-intensive products.

The most important tool used this research is Raman Spectroscopy with current advantages of high throuput, speed, sensitivity, spatial and spectral resolution and flexibiity. This thesis demonstrates the power of Raman Spectroscopy as a primary method for characterizing bio-based materials and facilitating their transformation into high-value products. The technique offers numerous advantages, including its non-invasive nature, rapid data acquisition, and versatility in analyzing a wide range of materials. While additional complementary techniques—such as X-ray Diffractometry (XRD), Scanning Electron Microscopy (SEM), and Infrared Spectroscopy (IR)—were also utilized to validate findings, Raman Spectroscopy proved to be the most efficient and effective method for monitoring material properties and optimizing product development.

Throughout this research, a variety of biomaterials have been explored, each with significant relevance across multiple fields. While the findings and developed applications hold substantial promise, there remains considerable potential for further refinement and optimization. Nevertheless, this work serves as a foundation for future research endeavors aimed at enhancing the valorization of biogenic resources. By demonstrating the efficacy of Raman Spectroscopy in this context, this study may inspire further investigations into the sustainable development of bio-based materials, ultimately driving innovation in waste utilization, material science, and biotechnology.

Structure of the thesis

This thesis is organized into three main chapters, each with a distinct focus and objective. Figure 1.2 presents a schematic display of the structure of the thesis.

The first chapter, titled " *Composition and morphology of biogenic carbonates as complex organic-mineral biomatrix revealed by current Raman technology and complementary techniques* " explores three different calcium carbonate-based biomaterials. The study has two main goals: (1) to enhance our understanding of the properties of these materials and (2) to showcase the capabilities of Raman Spectroscopy, alongside complementary techniques, in analyzing biogenic calcium carbonate structures.

The second chapter, " *Pharmaceutical formulations and novel drugs carrier developed from biogenic carbonate assisted by Raman technology,*" focuses on utilizing biogenic precursors to develop innovative pharmaceutical formulations. Throughout this chapter, Raman Spectroscopy and other analytical techniques serve as key tools for monitoring and optimizing drug formulations.

The third chapter, "*Biowaste Valorization: Conversion of Crab Shell-Derived Mg-Calcite into Calcium Phosphate Minerals Controlled by Raman Spectroscopy,*" investigates the transformation of biogenic calcium carbonate from waste crab shells into valuable calcium phosphate minerals. Raman Spectroscopy plays a central role in controlling and optimizing this conversion process.

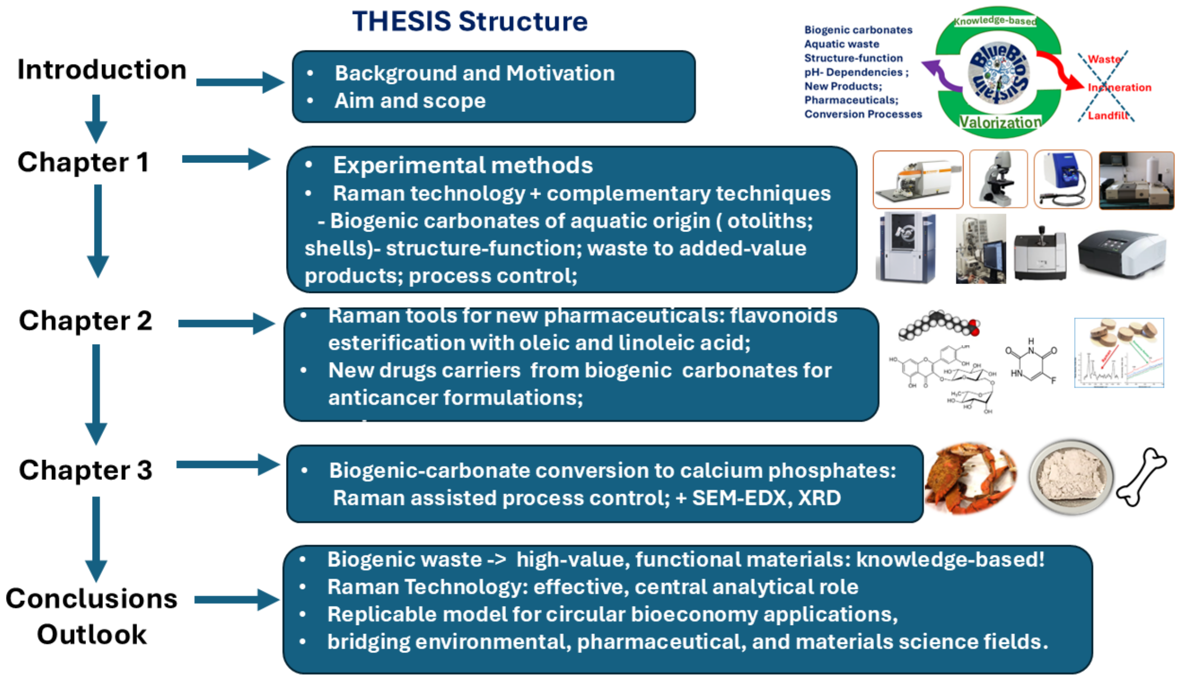


Figure 1.2 Schematic display of the structure of the thesis

1. Composition and morphology of biogenic carbonates as complex organic-mineral biomatrix revealed by current Raman technology and complementary techniques

1.1 Tracking the growing rings in biogenic aragonite from fish otolith using confocal Raman microspectroscopy and imaging

1.1.1 Background and aim

Otoliths, also known as "ear stones," are bioinorganic structures located in the inner ear of teleost fish. They play a crucial role in fish physiology, enabling balance, orientation, and sound detection [62-64]. Due to their unique composition, shape, and growth patterns, otoliths serve as essential tools in various scientific fields, including ichthyology, fisheries management, and environmental sciences [65-67].

Otoliths are composed primarily of aragonitic calcium carbonate and grow incrementally throughout a fish's life. Their growth occurs in discrete layers, which archive chronological data about the fish's life history and environmental conditions [68,69]. These structures exhibit periodic patterns, including daily, fortnightly, and monthly growth increments, making them valuable for age determination [51]. Otolith morphology varies among species, making them useful for taxonomic identification [70]. Otoliths serve essential sensory functions in fish, aiding in sound detection and spatial orientation. Their structure and function are closely related to the frequency sensitivity and directional hearing capabilities of fish [71]). The interaction between otoliths and sensory hair cells in the inner ear allows fish to perceive motion and vibrations, contributing to their ability to navigate aquatic environments effectively. The chemical composition of otoliths, including stable isotope ratios and trace element concentrations, provides valuable insights into fish physiology and environmental history. Carbon isotope records in otoliths can be used to infer a fish's position in the food chain and assess changes in its metabolic rate over time [72]. Otolith chemistry is widely employed to study fish migration patterns, habitat use, and exposure to environmental changes [72]. However, the assumptions underlying environmental reconstructions from otolith chemistry require critical assessment to ensure accurate interpretations [64]. Otolith analysis has become a fundamental technique in fisheries management. By integrating visual, chemical, and bioenergetic data, individual fish life history traits can be linked to physiological conditions [73]. Otolith chemistry has been recognized as a powerful tool for assessing fish environmental history, providing insights into habitat changes and population dynamics [73].

1.1.2 Results

This study investigated variations in crystallinity, structure, and composition along the growth axis of otoliths from gilthead seabream (Sparus aurata) inhabiting diverse environments, aiming to assess how spectroscopic and chemical signatures relate to life history and migratory behavior. Raman spectroscopy was employed to detect characteristic spectral bands, with Full Width at Half Maximum (FWHM) measurements used to analyze signal fluctuations. An increase in FWHM near the otolith core was observed, followed by a decline that exhibited two distinct minima aligned with growth ring structures. These patterns confirmed crystal discontinuities associated with annual rings and appeared to mirror individual activity cycles. While FWHM changes were not strongly correlated with environmental variables, differences in the slope of FWHM variation allowed clear separation between aquaculture/coastal specimens and those from open sea or estuarine habitats. Raman spectroscopy findings were further validated through Scanning Electron

Microscopy with Energy Dispersive X-ray Spectroscopy (SEM–EDX) and Laser Ablation Inductively Coupled Plasma Mass Spectrometry (LA-ICP-MS). SEM analysis supported the spectroscopic observations, while LA-ICP-MS data—particularly Ba/Ca ratios—enabled differentiation of individuals from aquaculture and transitional environments due to lower elemental variability. In contrast, greater variability was found in individuals from oligotrophic marine systems, likely reflecting fluctuating prey availability. These findings highlight the valuable role of Raman spectroscopy as a supplementary method for determining fish origin and migratory history, alongside traditional analytical techniques.

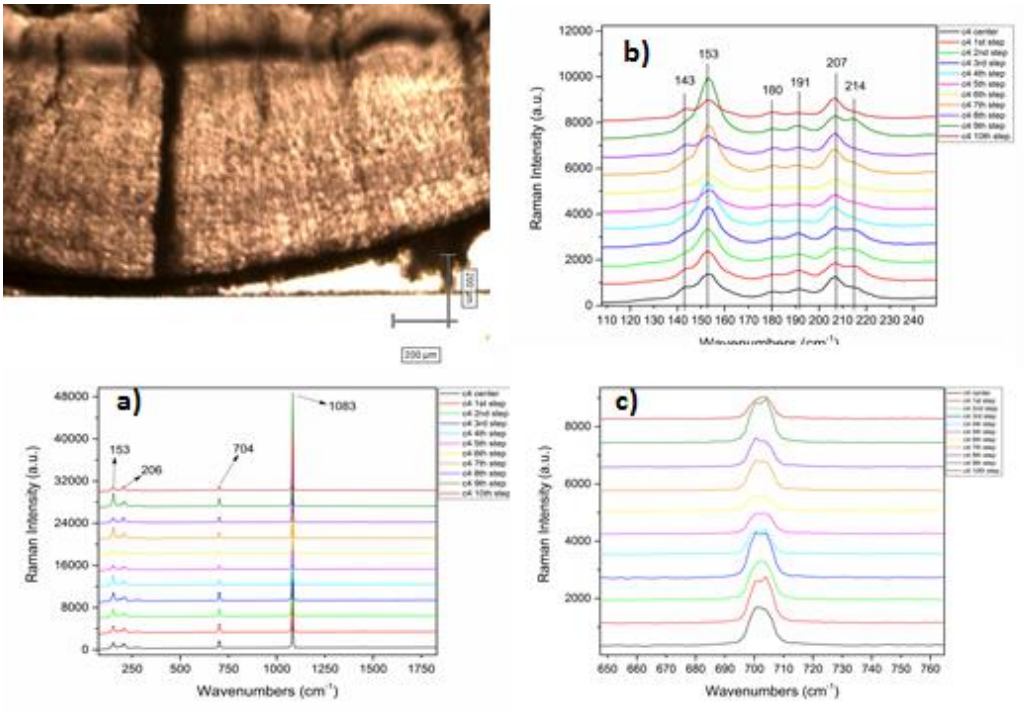


Figure 1.1.1 a) Typical Raman spectra collected from one otolith (C4) core to margin using constant lateral step controlled from Raman instrument stage and a 20 X objective; b), c) details of the spectral ranges containing the lattice modes (100-250 cm^{-1}) and the bending mode around 700 cm^{-1} of aragonite respectively showing slight changes from one step to another. Micrograph shows a fragment of the respective otolith where

the second ring is clearly visible. Taken from ref [6], ***G. Lazar****, F. Nekvapil, S. Matić-Skoko, et al., "Comparative screening the life-time composition and crystallinity variation in gilthead seabream otoliths Sparus aurata from different marine environments," Sci. Rep.,12, 9584, 2022, doi: 10.1038/s41598-022-13667-3.*

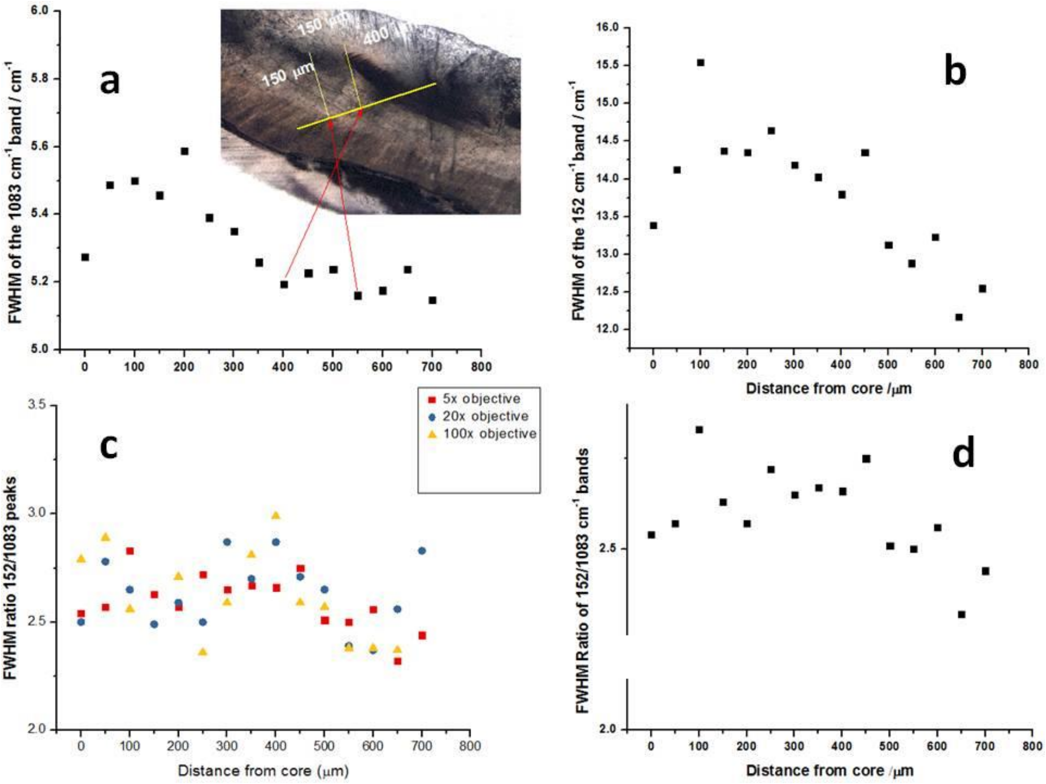


Figure 1.1.2 FWHM variation of the: (a) main carbonate band (1083 cm-1), (b) lattice mode at 152 (cm-1), (d) the ratio of the 1083 and 152 cm^{-1} bands, along the growth line. (c) Comparison of the FWHM ratio (152/1083 cm^{-1}), with different collecting objectives (5x, 20x and 100x). Taken from ref [6], ***G. Lazar****, F. Nekvapil, S. Matić-Skoko, et al., "Comparative screening the life-time composition and crystallinity variation in gilthead seabream otoliths Sparus aurata from different marine environments," Sci. Rep.,12, 9584, 2022, doi: 10.1038/s41598-022-13667-3.*

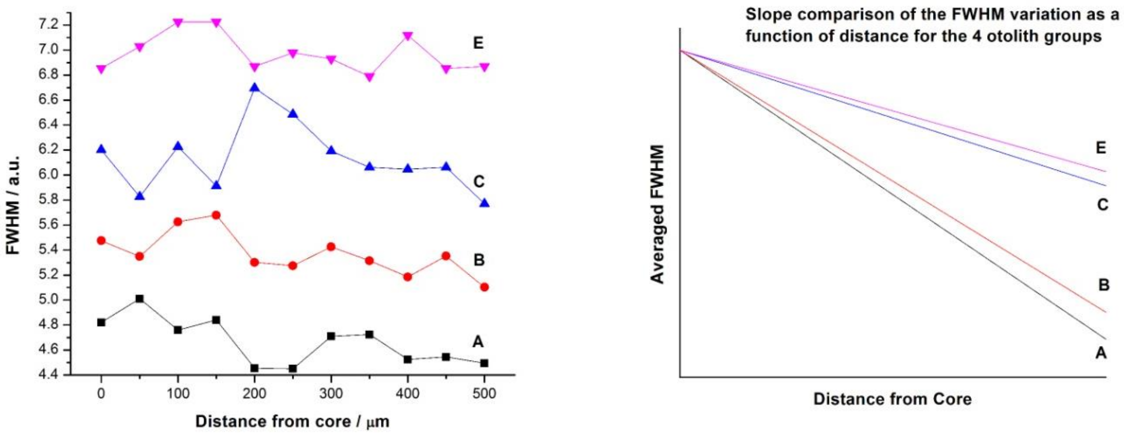


*Figure 1.1.3 (a) Comparative evolution of the FWHM of the main stretching mode of carbonate at 1083 cm^{-1} for the four main groups of otoliths, against the distance from core. (b) Slope comparison of the FWHM variation of the 4 distinct groups after averaging and linear fitting. Taken from ref [6], **G. Lazar**, F. Nekvapil, S. Matić-Skoko, et al., "Comparative screening the life-time composition and crystallinity variation in gilthead seabream otoliths Sparus aurata from different marine environments," Sci. Rep.,12, 9584, 2022, doi: 10.1038/s41598-022-13667-3*

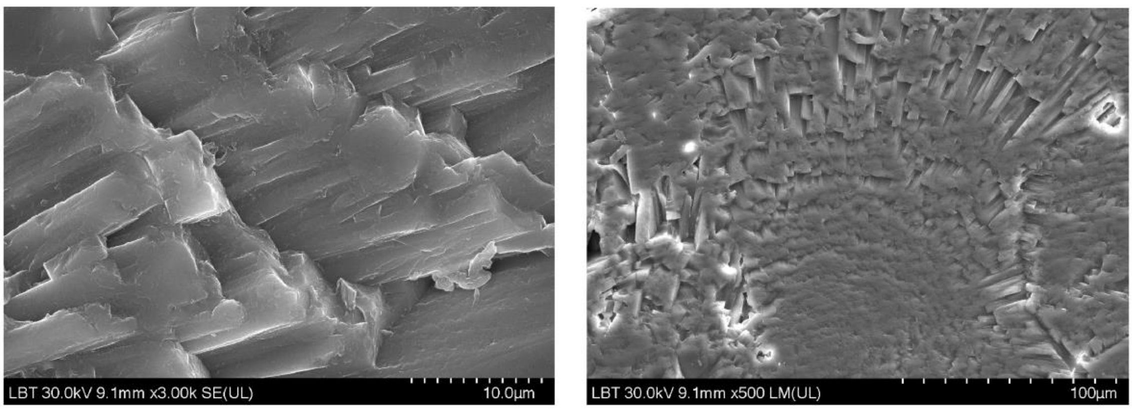


*Figure 1.1.4. Scanning Electron Microscopy images of a randomly selected otolith surface with different magnifications, revealing the needle-like aragonite crystal structure (left) and the radial crystal growth (left). Taken from ref [6], **G. Lazar**, F. Nekvapil, S. Matić-Skoko, et al., "Comparative screening the life-time composition and crystallinity variation*

in gilthead seabream otoliths Sparus aurata from different marine environments," Sci. Rep.,12, 9584, 2022, doi: 10.1038/s41598-022-13667-3.

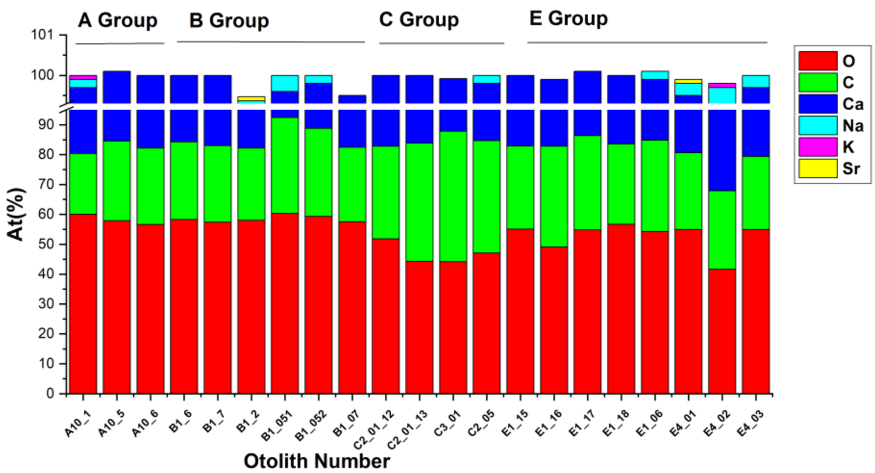


Figure 1.1.5. EDX comparative data on the four otolith groups showing the atomic weight At (%) plotted for O, C, Ca, Na, K and Sr. Taken from ref [6], ***G. Lazar****, F. Nekvapil, S. Matić-Skoko, et al., "Comparative screening the life-time composition and crystallinity variation in gilthead seabream otoliths Sparus aurata from different marine environments," Sci. Rep.,12, 9584, 2022, doi: 10.1038/s41598-022-13667-3.*

1.2 Effects of ocean acidification on the morphology and structure of Hexaplex trunculus sea snail shell by Raman Spectroscopy, XRD and SEM

1.2.1 Background

Ocean acidification is a growing threat to marine ecosystems, with profound implications for biodiversity and biogeochemical processes [74-76]. It is primarily caused by the ocean's absorption of atmospheric CO_2, which forms carbonic acid upon dissolution. This acid dissociates into bicarbonate and hydrogen ions, lowering seawater pH and increasing acidity. Human activities, particularly fossil fuel combustion and deforestation, have significantly raised atmospheric CO_2 to levels unprecedented in recent history. Projections estimate concentrations may exceed 1000 ppm by 2100, resulting in a pH decline of 0.3–0.4 units [77].

Marine organisms that rely on calcium carbonate ($CaCO_3$) for shell or skeletal structures are particularly susceptible. Responses vary based on factors like the presence of $CaCO_3$-based structures, the crystal polymorph (aragonite or calcite), and developmental stage [78]. Mollusks, for instance, form shells composed of crystalline $CaCO_3$ embedded in an organic matrix. Typically, these shells include an inner nacreous layer (aragonite), a middle transitional layer, and an outer prismatic layer of aragonite or calcite [79,80]. Shell formation is controlled by the organic matrix synthesized in the extrapallial space, which directs crystal nucleation and growth [81-83]. This intricate process gives mollusk shells remarkable mechanical properties, often superior to synthetic composites [83].

One species of interest is *Hexaplex trunculus* (Linnaeus, 1758), or the banded dye-murex, a gastropod of ecological and historical importance. Its aragonitic shell contains organic compounds and pigments that give it a distinct coloration. Historically valued for its purple dye, *H. trunculus* has not been extensively studied in relation to ocean acidification.

This study explores how simulated acidified seawater—reflecting future ocean pH scenarios—affects the shell morphology and integrity of *H. trunculus*. Using Raman Spectroscopy, Scanning Electron Microscopy (SEM), and X-Ray Diffractometry (XRD), we assess changes in mineral composition, crystalline structure, and shell microarchitecture. These techniques offer high sensitivity and resolution, providing deeper insight into the species' potential vulnerability to future ocean conditions.

1.2.2 Results

The effect of a range of pH conditions relevant in the context of ocean acidification on the H. trunculus shells were studied using Raman Spectroscopy, Scanning Electron Microscopy (SEM), as well as X-Ray Diffractometry (XRD). Specimens originating from environments with the pH ranging from 8.1 to 7.4 were studied, to replicate the expected future ocean acidification. The snails are mainly composed of a $CaCO_3$ backbone, and organic pigments. In terms of the $CaCO_3$ polimorph, the *H. trunculus* is mainly composed of aragonite, both the Raman spectra and XRD data however, revelead specimens containing calcite traces, at pH 8.0-7.8. In order to study the effect of pH on the morphology we compared the Raman and XRD spectral properties, of the snail individuals as a function of the environmental pH. Using these properties, we compared the relative crystallinity of the biogenic calcium carbonate at the various pH values. The crystallinity was relatively constant on the interior of the shells, with larger variations being visible on the exterior, suggesting a higher pH sensitivity on the exterior of the shells, as expected. Moreover, the XRD data suggests that the presence or absence of calcite in the crystalline structure does not directly influence the crystallinity of the calcium carbonate. The SEM-EDX data was then correlated with the Raman spectra to accurately determine the pH influence on the morphology.

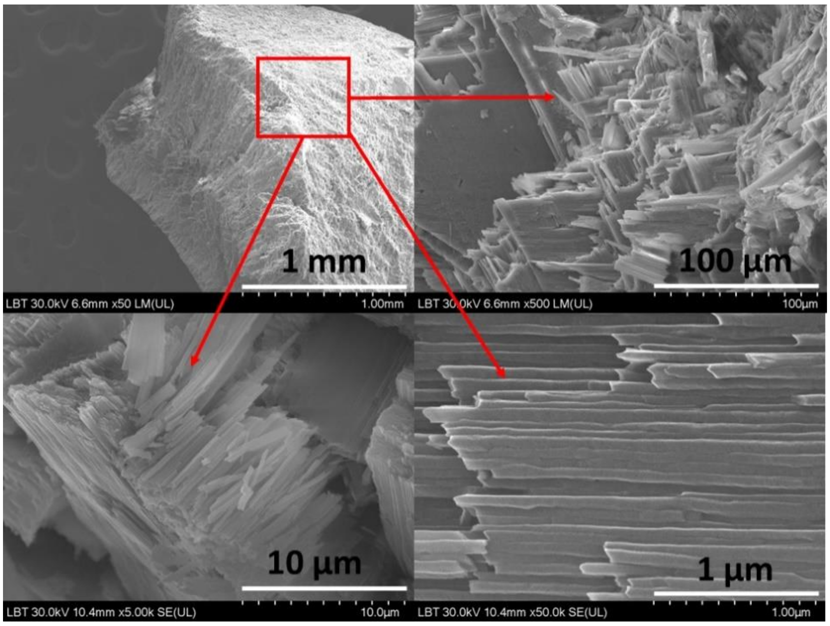


Figure 1.2.1. High resolution SEM images of the H. trunculus specimens' surface

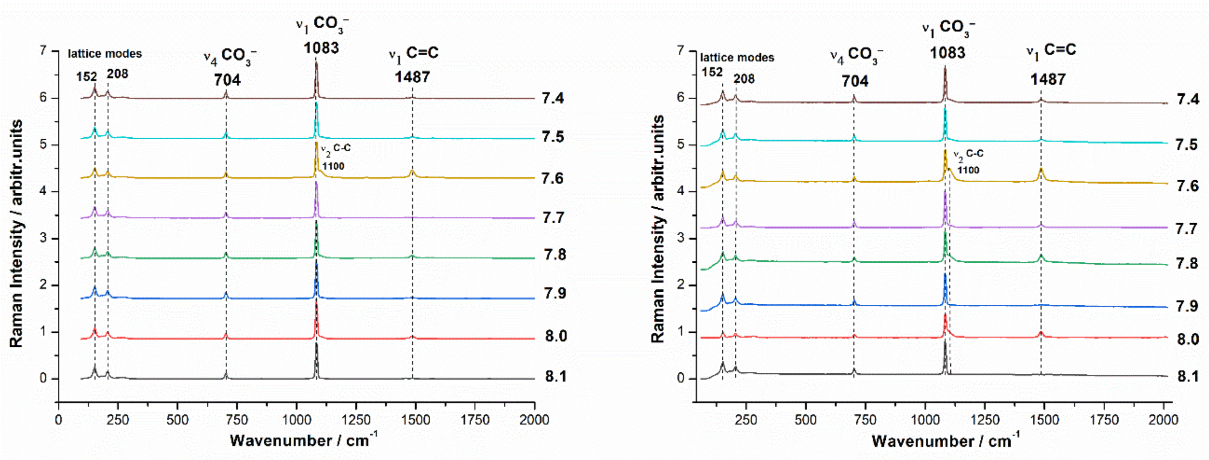


Figure 1.2.2 Stacked raman spectra of H.Trunculus shells both on the interior (left) and exterior (right) for each pH value with the main Raman bands marked

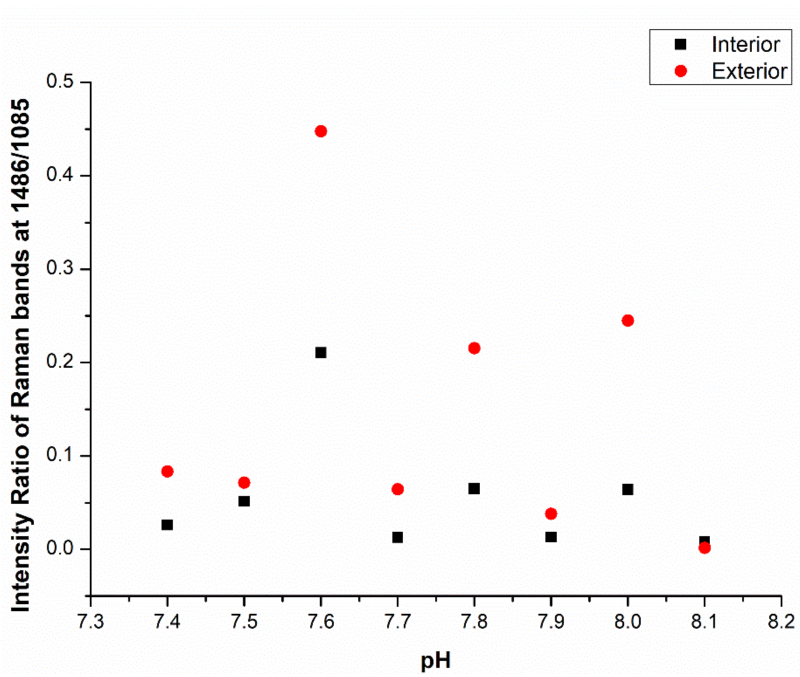
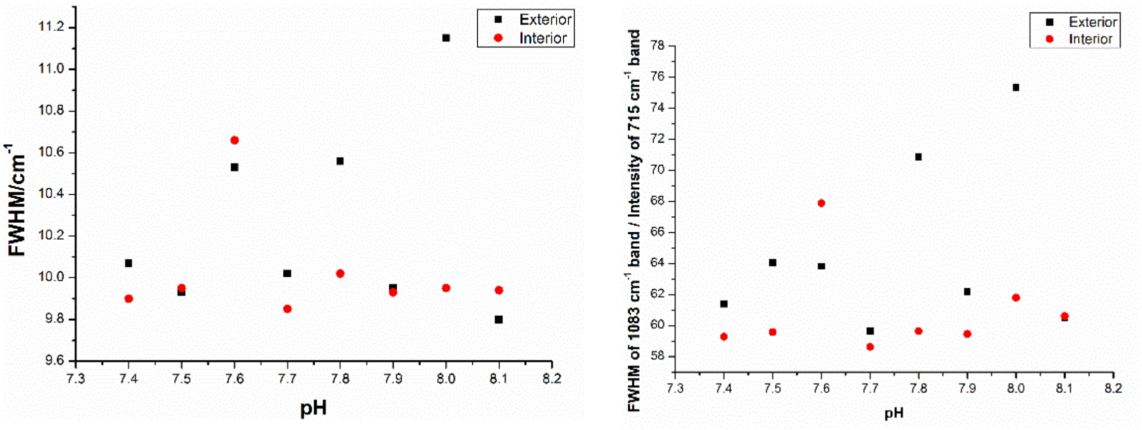


Figure 1.2.3. Intensity Ratio of the Raman bands at 1486 and 1085 cm^{-1}



a **b**

Figure 1.2.4 FWHM of the main carbonate band on the exterior and interior for different pH values (a). The ratio of FWHM of the main carbonate band and the intensity of the 715 band for each pH value (b).

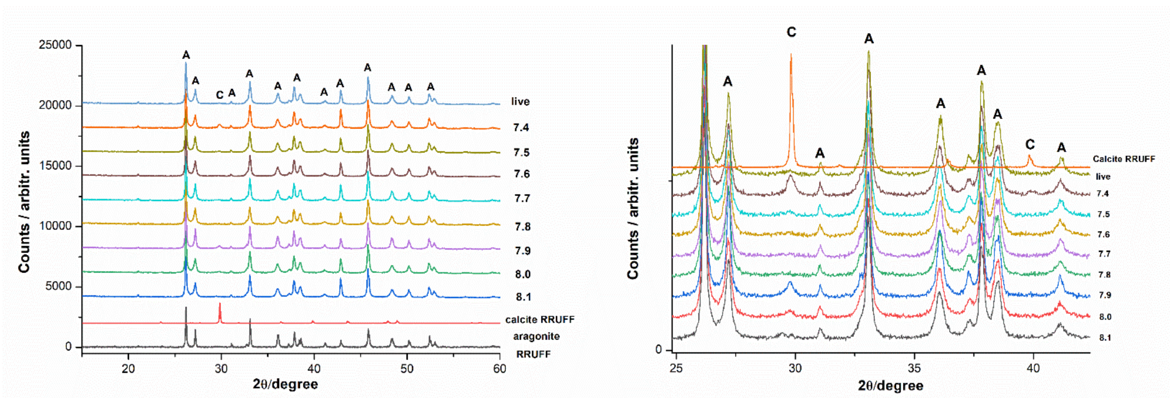


Figure 1.2.5 Stacked XRD spectra of H.trunculus shells for each expected environmental pH value, zoomed in on the 2 main aragonite peaks used in further determinations.

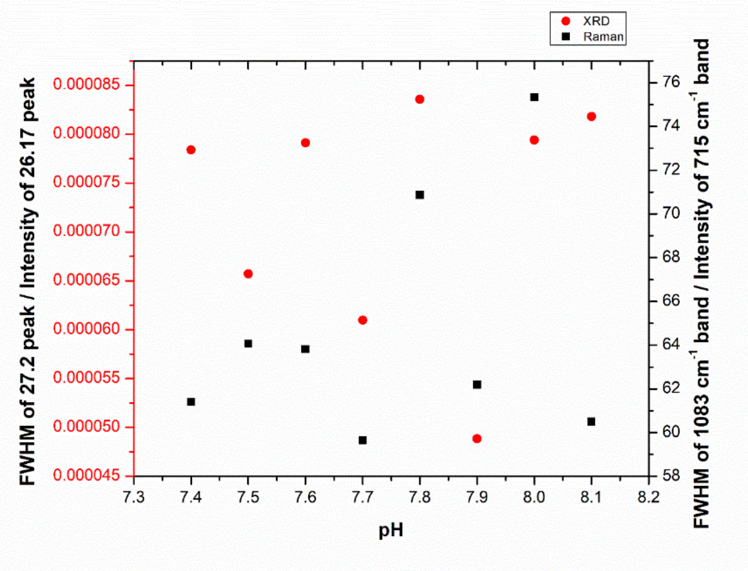


Figure 1.2.6. Combined plot of both the Ratio of the FWHM of the 27.2⁰ peak and the intensity of 26.17⁰ peak (XRD) and the Ratio of the FWHM of the main carbonate band at 1083 cm-1 and the relative intensity of the 704 cm-1 carbonate band (Raman) as a function of environmental pH.

1.3 Rapid assessment tool for biogenic powders from crustacean shell waste by FTIR complemented with X-ray diffraction, SEM, NMR

1.3.1. Background and aim of the study

Crustacean shells, often discarded as industrial waste, are gaining recognition for their potential in sustainable applications due to their unique structure and bioactive components. Rich in chitin and its derivative chitosan, these shells can be transformed into high-value materials used in biodegradable plastics, water purification, and food packaging [7,57, 84-86]. Chitosan, in particular, serves as an effective natural adsorbent for removing pollutants such as heavy metals and phosphates from wastewater [87-90].

In agriculture, crab shells act as natural soil amendments, offering an eco-friendly alternative to chemical fertilizers [90]. The food industry also utilizes shell-derived bioactive compounds like chitooligosaccharides for their antimicrobial and anti-inflammatory properties [91].

Structurally, shells from species like Callinectes sapidus and Carcinus aestuarii contain biogenic calcite with a Bouligand-type nanostructure, contributing to their strength and functionality [1,2,7]. These nanostructures also interact with pigments, providing color-specific features that open avenues in materials science and nanotechnology.

Given their properties, biogenic calcium carbonate from crustacean shells is a promising base for developing pharmaceutical and biomedical materials. This study explores how milling and deproteinization affect shell powder structure and suitability for such applications.

1.3.2 Results

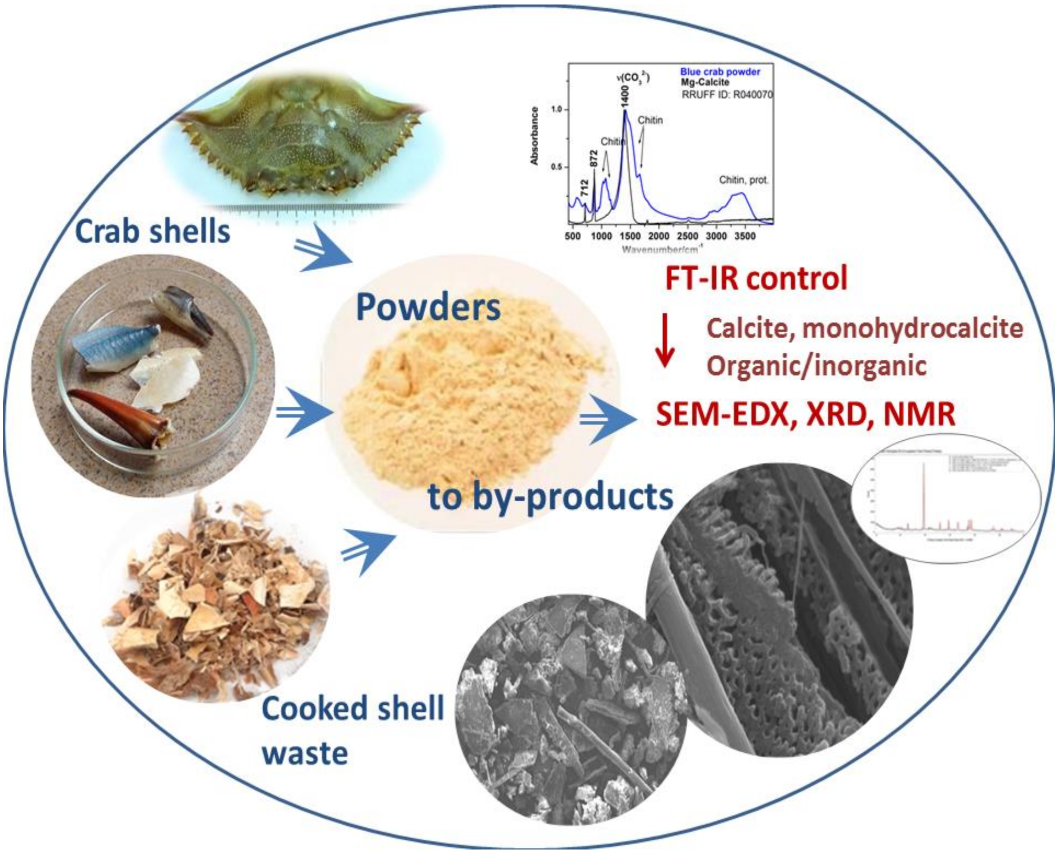


*Figure 1.3.1. Summary display of the experimental approach for tracking biogenic waste processing from the raw material to waste powder composition using FTIR, supported by SEM–EDX, NMR, and XRD. Taken from ref [8], L. Ogresta, F. Nekvapil, T. Tǎmaş, L. Barbu-Tudoran, M. Suciu, R. Hirian, M. Aluaş, **G. Lazar**, E. Levei, B. Glamuzina, and S. C. Pinzaru, "Rapid and Application-Tailored Assessment Tool for Biogenic Powders from Crustacean Shell Waste: Fourier Transform-Infrared Spectroscopy Complemented with X-ray Diffraction, Scanning Electron Microscopy, and Nuclear Magnetic Resonance Spectroscopy" ACS Omega, 6, 42, 27773–27780, 2021, doi: 10.1021/acsomega.1c03279.*

Crustacean shell waste, due to its high content of calcium carbonate, chitin, proteins, pigments, and its nanoporous architecture, holds considerable promise for diverse applications. With vast amounts of shell waste generated each year, these materials represent a sustainable and renewable source for producing eco-friendly, value-added biogenic products. This study introduces an infrared (IR)-based method to distinguish between different biogenic powders derived from both raw and food-processed crustacean shells. The technique's reliability was verified through complementary analyses including X-ray diffraction (XRD), nuclear magnetic resonance (NMR), and scanning electron microscopy with energy-dispersive X-ray spectroscopy (SEM–EDX).

The research focused on examining how two common treatments—alkaline deproteinization and mechanical milling—affect the physical and chemical properties of crab shell waste. Findings revealed that deproteinization using sodium hydroxide could be identified by monitoring the IR absorbance intensity ratio between the $\upsilon(CH_{2,3})$ and $\upsilon\_asym(CO_3^{2-})$ bands. While milling had a lesser impact on this ratio, it significantly influenced particle size distribution and surface morphology. Additionally, variations in the organic-to-inorganic content were observed among shells of different colors. Interestingly, samples stored for over six months contained monohydrocalcite, a hydrated form of calcium carbonate, which was not present in freshly processed shells. The deproteinization process also altered the mechanical characteristics of the shells, making them more brittle and resulting in a higher yield of fine particles after grinding.

2. Pharmaceutical formulations and novel drugs carrier developed from biogenic carbonate assisted by Raman technology

2.1 Development of Flavonoid Prodrugs: Enhancing Bioavailability and Stability for Pharmaceutical Formulations

2.1.1 Background

Flavonoids are a large group of plant-derived polyphenols found in fruits, vegetables, herbs, and beverages, known for their antioxidant, anti-inflammatory, and anticancer properties [101-103]. Despite their therapeutic potential, many flavonoids suffer from poor bioavailability due to low solubility, limited absorption, and rapid metabolism [104-106]. To overcome these limitations, prodrug strategies—particularly lipophilic derivatization using fatty acids—have been explored to enhance stability and absorption [107,108].

Rutin (RUT), a flavonol with strong bioactivity, is hindered by its hydrophilic nature, limiting topical and systemic use [109]. Conjugation with unsaturated fatty acids (UFAs) such as oleic acid (OA) and linoleic acid (LA) not only improves RUT's pharmacokinetics but also protects UFAs from oxidation [110-112]. Similarly, silibinin (SIL), the main bioactive of *Silybum marianum*, has recognized hepatoprotective effects but also faces bioavailability issues [112-116]. Lipid-based prodrugs of SIL have shown improved absorption and efficacy [116].

This study investigates the synthesis, characterization, and safety of rutin and silibinin conjugates with OA and LA—RUT-O, RUT-L, SIL-O, and SIL-L—as potential nutraceuticals. By enhancing their physicochemical properties, these bioconjugates may provide more effective treatments for liver, cardiovascular, and skin disorders. FT-Raman is used to confirm the synthesis o bioconjugates, e rutin oleate, rutin linoleate and silibinin oleate, silibinin linoleate bioconjugates.

2.2.2 Rutin bioconjugates as potential nutraceutical prodrugs Raman tools to proof esterification with oleic and linoleic acid

The FT-Raman spectra of RUT, OA, and RUT-O are shown in Figure 2.2.1, with the RUT-L spectra presented in Figure 2.2.2. As expected, the bioconjugates (RUT-O and RUT-L) display characteristic bands from both the parent flavonoid (RUT) and fatty acids (OA or LA), with slight shifts indicative of ester formation. These findings are consistent with literature data [114,115].

In the fingerprint region (1,000–1,800 cm^{-1}), six prominent bands in RUT-O correspond to vibrations from both RUT and OA, showing minor shifts in position. Below 800 cm^{-1}, RUT-O exhibits skeletal ring vibrations from RUT, with no significant OA contributions. In the high-frequency region (~3,000 cm^{-1}), overlapping O–H stretching bands from RUT and OA are evident, with intensity and position changes confirming their combined presence. Similar spectral patterns were observed for RUT-L due to the structural similarity between OA and LA (Figure 2.2.2).

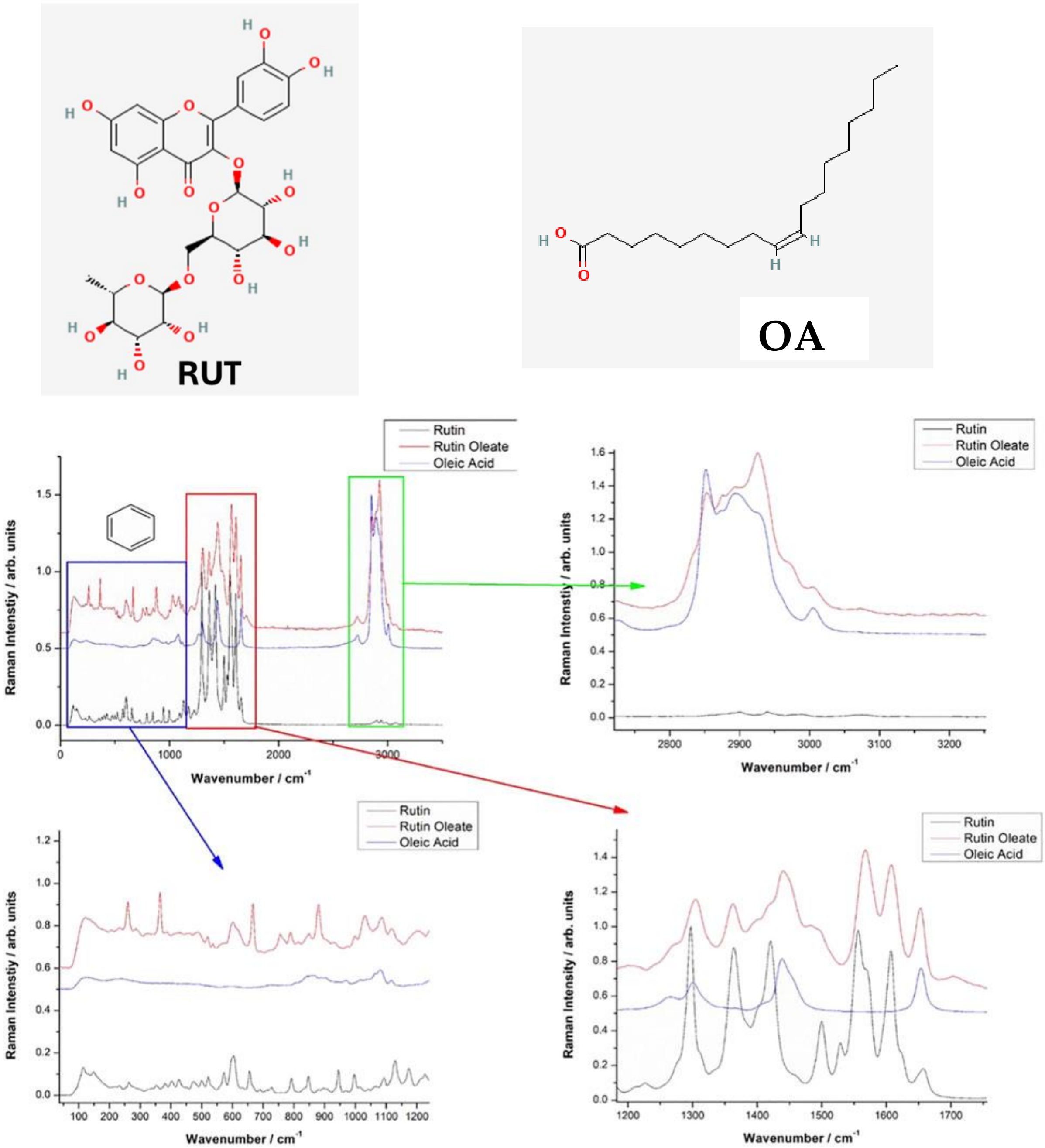


*Figure 2.2.1. Comparative Raman spectra of Rutin (RUT), Oleic acid (OA) and Rutin oleate (RUT-O) (bottom), along with the 2D molecular structure of RUT (top left) and OA (top right). Adapted from ref [9], C. A. Dehelean, D. Coricovac, I. Pinzaru, I. Marcovici, I. G. Macasoi, A. Semenescu, **G. Lazar**, S. Pinzaru, I. Radulov, E. Alexa, O. Cretu, "Rutin bioconjugates as potential nutraceutical prodrugs: An in vitro and in ovo toxicological screening," Front. Pharmacol., 13, 2022, doi: 10.3389/fphar.2022.1000608.*

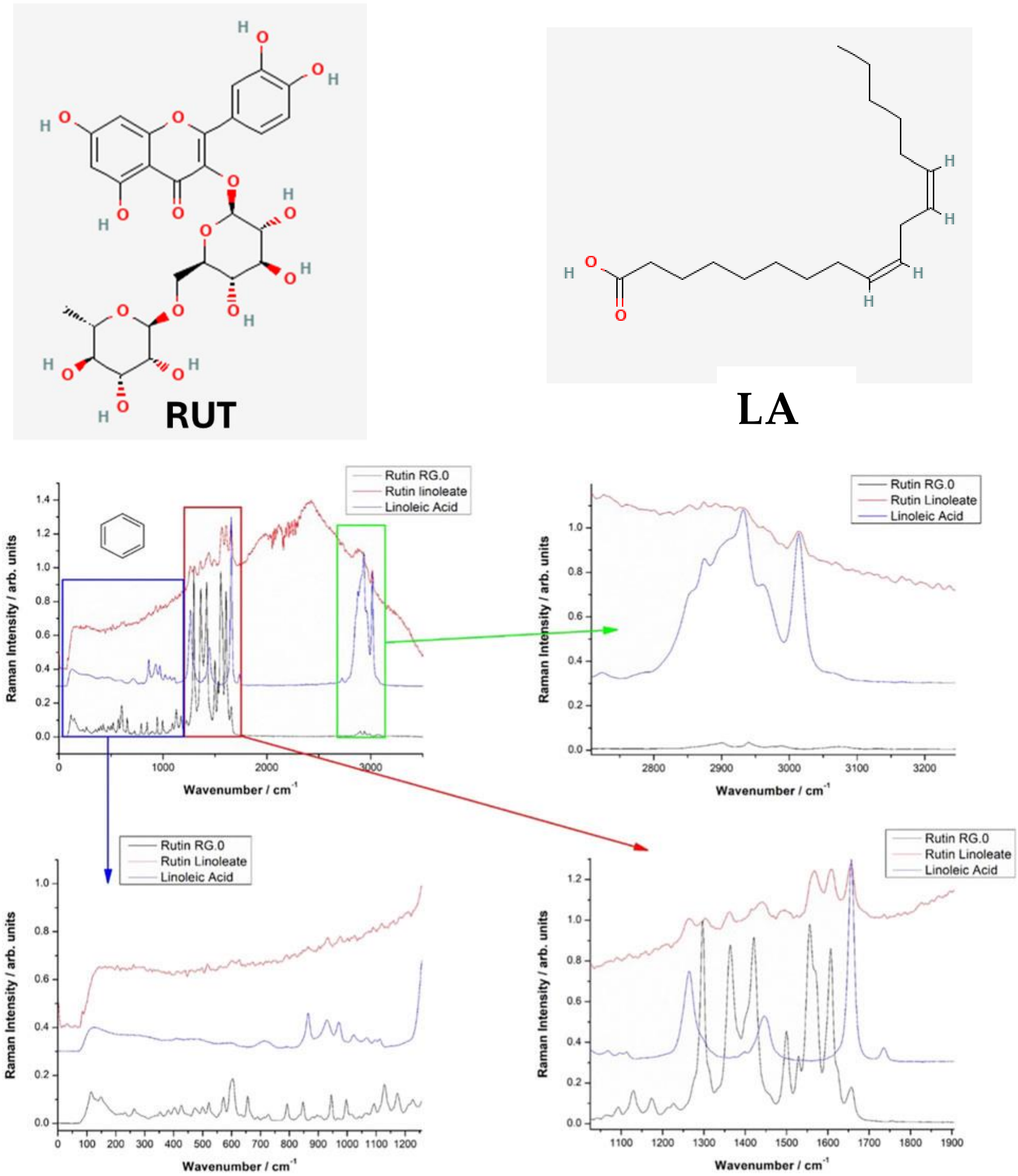


*Figure 2.2.2 Comparative Raman spectra of Rutin (RUT), Linoleic acid (LA) and Rutin linoleate (RUT-L), (bottom), along with the 2D molecular structure of RUT (top left) and LA (top right). Adapted from ref [9] C. A. Dehelean, D. Coricovac, I. Pinzaru, I. Marcovici, I. G. Macasoi, A. Semenescu, **G. Lazar**, S. Pinzaru, I. Radulov, E. Alexa, O. Cretu, "Rutin bioconjugates as potential nutraceutical prodrugs: An in vitro and in ovo toxicological screening," Front. Pharmacol., 13, 2022, doi: 10.3389/fphar.2022.1000608.*

2.2.3 Silibinin bioconjugates as potential nutraceutical prodrugs; Raman tools to proof esterification with oleic and linoleic acid

The FT-Raman spectra for the parent compounds (SIL, OA, and LA) and their derivatives (SIL-O, SIL-L) are shown in Figures 2.2.3 and 2.2.4. The main Raman bands for OA are observed in the 1200–1700 cm−1 region, including a 1265 cm−1 band (═C–H deformation), a 1300 cm−1 band (C–H bending), a 1440 cm−1 band (C–H scissoring), and a 1655 cm−1 band (C═C stretching). In LA, small shifts are seen, with the scissoring band at 1450 cm−1 and the stretching band at 1657 cm−1, along with a new 1735 cm−1 band for the (C═O) stretch. In the 2800–3200 cm−1 region, both acids show C–H stretching bands, with differences in intensity and position. OA's main bands are at 2727, 2848, 2893, and 3003 cm−1, while LA has bands at 2848, 2875, 2893, 2931, 2961, and 3014 cm−1.

The spectra of the oleate/linoleate derivatives are dominated by the parent compound bands, with small shifts indicating changes in vibrational modes. For SIL-O, in the 0–2000 cm−1 range, three bands (890, 1551, 1711 cm−1) not present in SIL or OA are observed, with the 1711 cm−1 peak corresponding to the ester C=O stretch. The C=C stretching band shifts from 1655 cm−1 in OA to 1648 cm−1 in SIL-O. The C–H stretching bands in the 2800–3200 cm−1 region show small shifts and intensity changes, and some intense peaks from the parent compounds (3005 cm−1 in OA and 3059 cm−1 in SIL) are absent in SIL-O. In contrast, SIL-L retains bands in the 1000–2000 cm−1 range that correspond to those in SIL or LA, with slight shifts. The C═C stretch appears at 1652 cm−1 in SIL-L (compared to 1657 cm−1 in LA), and the C═O stretch at 1735 cm−1 in LA appears as a weak shoulder at 1732 cm−1 in SIL-L.

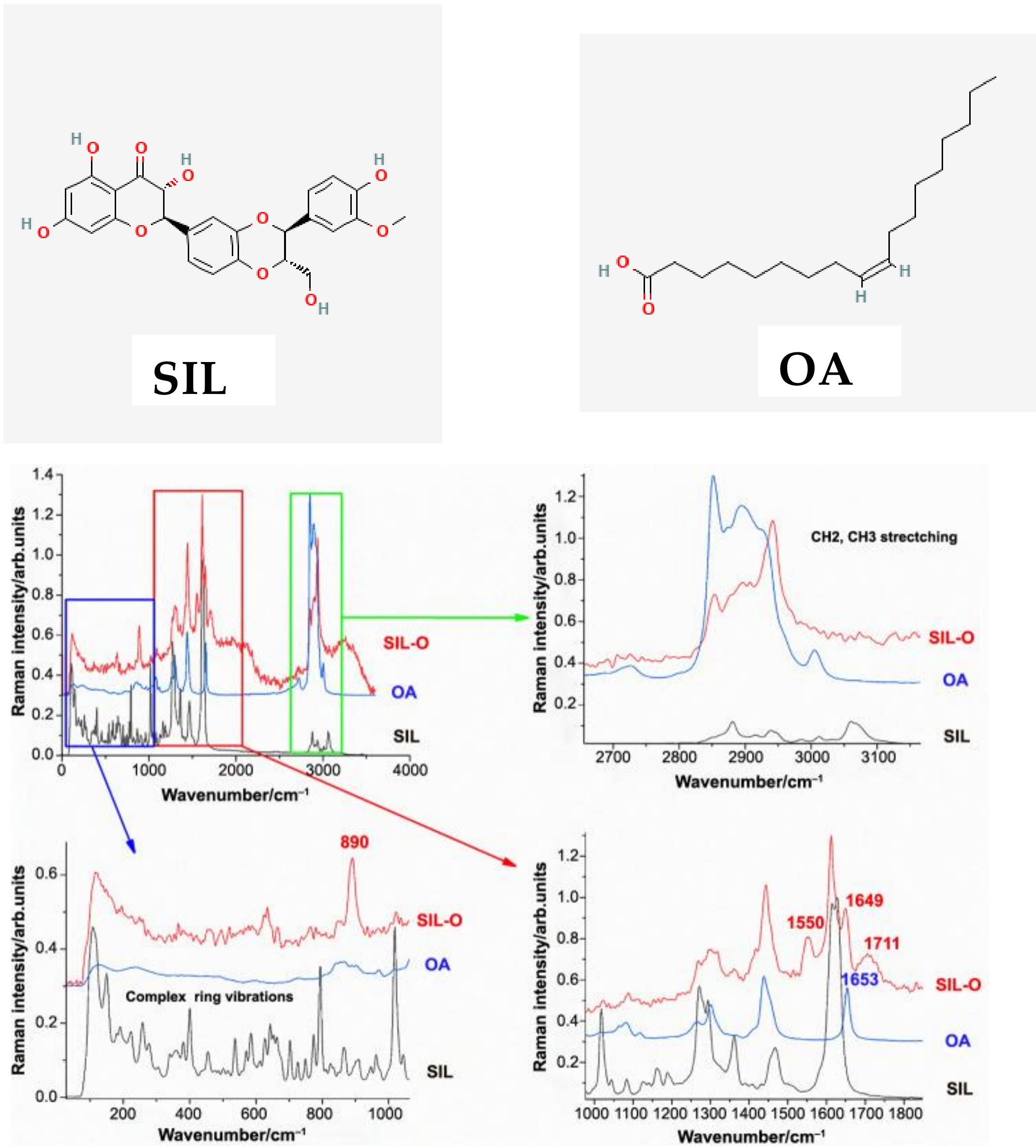


Figure 2.2.3 Comparative FT–Raman spectra of silibinin, oleic acid, and silibinin oleate. Excitation: 1064 nm. SIL: Silibinin; OA: Oleic acid; SIL-O: Silibinin oleate. (bottom), along with the 2D molecular structure of SIL (top left) and OA (top right). Adapted from ref [10], Cristina Dehelean, Ersilia Alexa, Iasmina Marcovici, Andrada Iftode, ***Geza Lazar****, Andrea Simion, Vasile Chis, Adrian Pirnau, Simona Cinta Pinzaru, Estera Boeriu: "Synthesis, Characterization, and in vitro–in Ovo Toxicological Screening of Silibinin Fatty Acids Conjugates As Prodrugs With Potential Biomedical Applications". 2024. Biomolecules and Biomedicine 24 (6): 1735–1750. https://doi.org/10.17305/bb.2024.10600.*

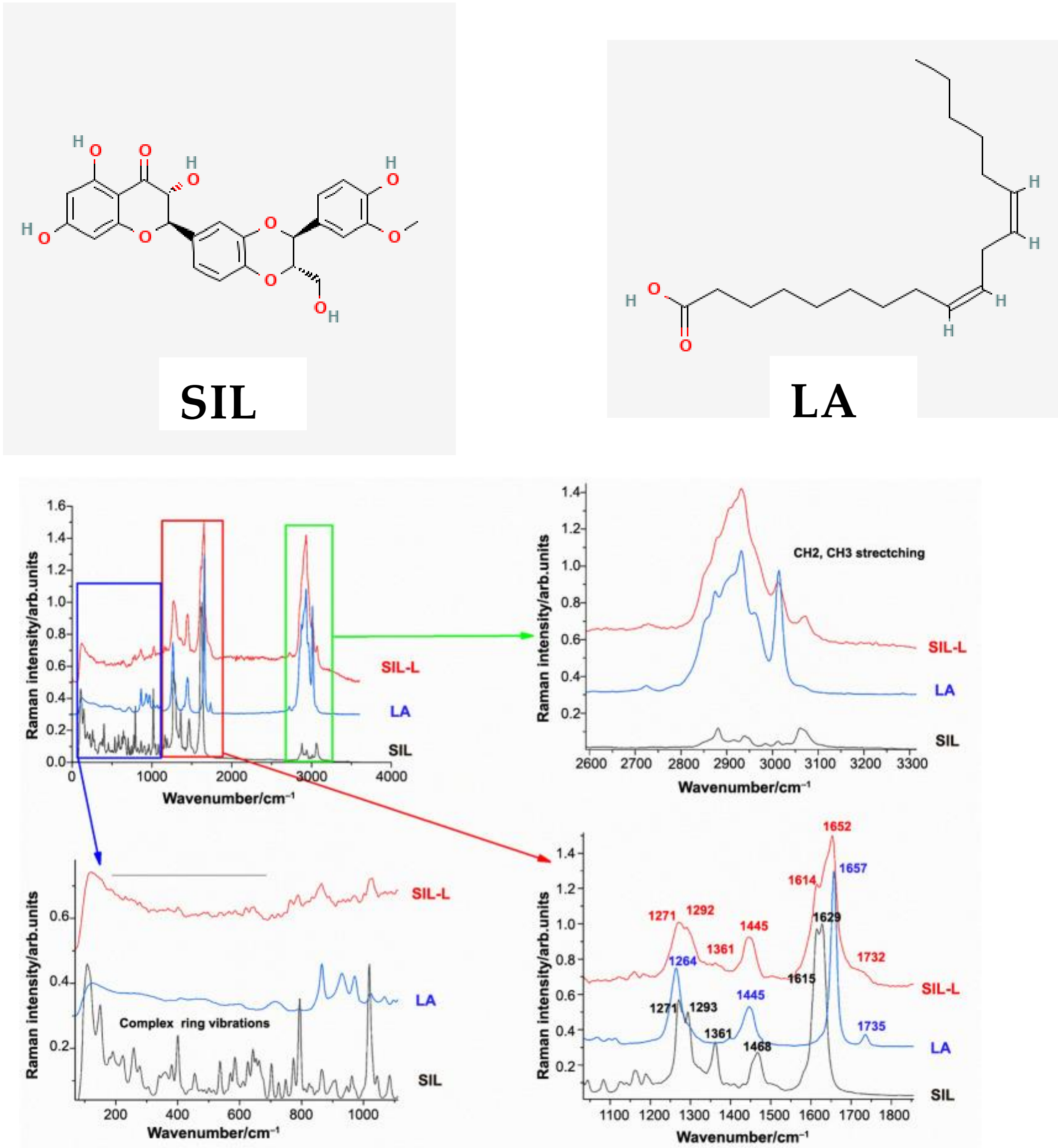


Figure 2.2.4 Comparative FT–Raman spectra of silibinin, linoleic acid, and silibinin linoleate. Excitation: 1064 nm. SIL: Silibinin; LA: Linoleic acid; SIL-L: Silibilin linoleate (bottom), along with the 2D molecular structure of SIL (top left) and LA (top right). Adapted from ref [10] Cristina Dehelean, Ersilia Alexa, Iasmina Marcovici, Andrada Iftode, ***Geza Lazar****, Andrea Simion, Vasile Chis, Adrian Pirnau, Simona Cinta Pinzaru, Estera Boeriu: "Synthesis, Characterization, and in vitro–in Ovo Toxicological Screening of Silibinin Fatty Acids Conjugates As Prodrugs With Potential Biomedical Applications". 2024. Biomolecules and Biomedicine 24 (6): 1735–1750. https://doi.org/10.17305/bb.2024.10600*

2.3 Novel biogenic calcium carbonate based drug carrier

2.3.1 Background

5-Fluorouracil (5-FU) is a widely used chemotherapeutic agent for treating various cancers, but its clinical effectiveness is limited by factors such as poor bioavailability, a short plasma half-life, and drug resistance [117,118]. To overcome these challenges, research has focused on drug delivery systems that enhance drug stability, bioavailability, and targeted delivery. Various nanocarriers, including lipid-based, polymeric, and inorganic nanoparticles, have shown potential in improving 5-FU therapy. For instance, chitosan-based nanoparticles enhance drug stability and cellular uptake, while poly(lactic-co-glycolic acid) (PLGA) formulations provide sustained release, addressing rapid metabolism and fluctuating bioavailability [133-142]. Inorganic nanoparticles, such as chitosan-modified carriers and amine-functionalized silica nanoparticles, also improve 5-FU delivery, reducing side effects and enhancing therapeutic outcomes [140-142].

Despite its effectiveness, 5-FU causes significant off-target toxicity, including cardiovascular complications and gastrointestinal damage [143-145]. To mitigate these side effects, biogenic calcium carbonate nanoparticles from sources like cockle shells have been explored for targeted drug delivery, showing promise in improving specificity and reducing toxicity in anticancer treatments, including 5-FU [146-148].

This section focuses on developing a novel 5-FU formulation using biogenic calcite from waste blue crab shells as a drug carrier. The 3D porous structure of the material allows for efficient drug loading, and the formulation is designed in tablet form. Raman Spectroscopy, XRD, and SEM are used to characterize the composite's structural and morphological properties, while Surface-Enhanced Raman Spectroscopy (SERS) monitors the drug release in different environments.

2.3.2 Results

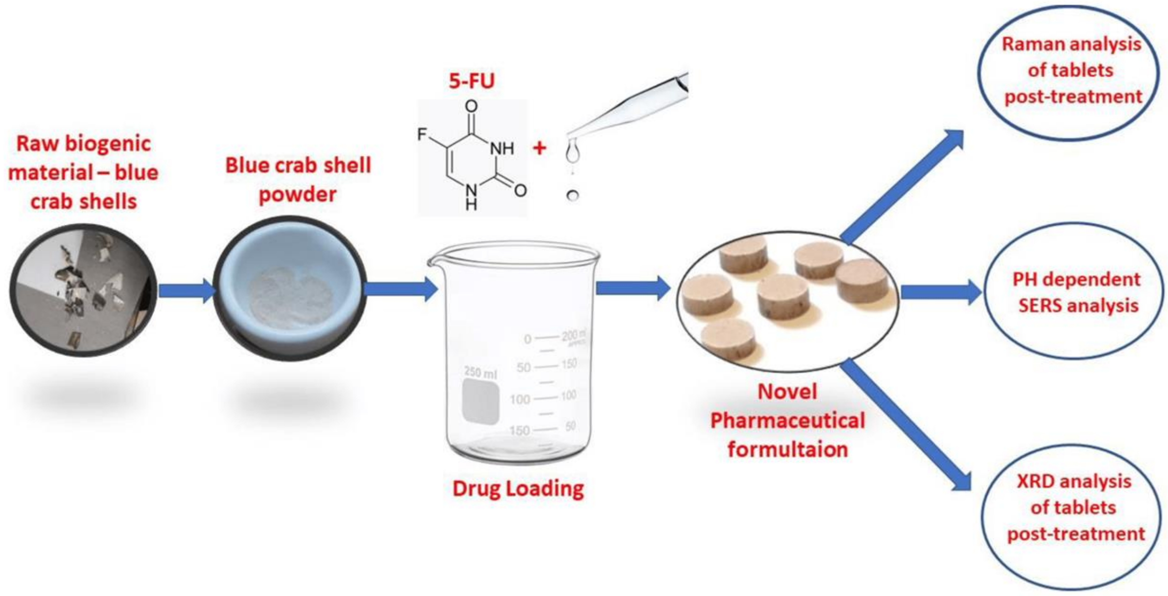


*Figure 2.3.1 Schematic design of the biogenic calcite drug carrier for loading the 5-FU and the pH effect on the tablet and its slow-releasing active ingredient. Taken from ref [2], **G. Lazar**, F. Nekvapil, B. Glamuzina;T. Tamaș, L. Barbu-Tudoran, M. Suciu, and S. Cinta Pinzaru. "pH-Dependent Behavior of Novel 5-FU Delivery System in Environmental Conditions Comparable to the Gastro-Intestinal Tract," Pharmaceutics, 15, 1011, 2023, doi: 10.3390/pharmaceutics15031011.*

This study confirms the effectiveness of biogenic calcium carbonate from blue crab shells as a drug carrier in relevant pH environments. Our findings validate the material's viability, showing that the novel pharmaceutical formulation retains its properties even in acidic conditions, similar to those found in the digestive tract. The slow drug release in acidic environments ensures reduced cytotoxic side effects, despite only ~40% of the 5-FU being released under these conditions. The tablet size and dosage can be adjusted to meet specific needs. Though the tablet surface may deteriorate slightly under acidic exposure, the release process remains largely unaffected.

The use of blue crab shells as carriers offers several advantages over other formulations, including biocompatibility, minimal side effects, and antioxidant benefits from the carotenoid content. The drug loading process is simple, requiring little physical preparation or expensive equipment, making it scalable for industrial use. Additionally, using crab shells aligns with circular economy and blue bioeconomy principles, as they are a readily available waste material.

3. Biowaste valorisation: Conversion of Crab Shell-Derived Mg-Calcite into Calcium Phosphate Minerals Controlled by Raman Spectroscopy

3.1 Background and aim

In recent times, sustainable biomaterials technologies have garnered significant scientific attention. The prospect of converting biogenic waste into high-value products has fuelled many recent innovations [85-153,154] within blue bioeconomy concept. Among these products, calcium phosphates play pivotal roles in various industrial and biomedical applications. For instance, calcium phosphates are employed in water treatment processes [155-157]; in the food industry, calcium phosphates serve multiple roles in food processing [158,159]; while in agriculture, these minerals are processed into fertilizers that supply essential phosphorus for plant growth [160-162]. In biomedicine, calcium phosphate-based biomaterials are extensively used in orthopaedics and dentistry for bone grafts and implants due to their biocompatibility and structural similarity to natural bone, which facilitate osteoconduction and support new bone formation [163-167]. Although hydroxyapatite (HA), beta-tricalcium phosphate (β-TCP), and brushite are the most popular bone substitution materials, recent studies have demonstrated the viability of other calcium phosphates such as monetite or whitlockite [168-174]. Despite a growing body of research on calcium phosphates, only a small fraction of published papers focus on their application as bone replacement materials, and an even smaller portion investigate the use of biogenic calcium carbonate sources as precursors for calcium phosphate [175-178] .

In the present work, we propose the use of an abundant yet scarcely utilized biomaterial—wasted post-consumption crab shells—as a precursor for conversion into calcium phosphate.

Biogenic carbonate derived from crustaceans exploitation is a promising material with wider applicability, due to their amazing nanoarchitecture as 3d plywood -like Bouligand pattern which naturally supply nanochannels and nanopores in the mineral-organic composite [2,3,7,8, 85]. Moreover, their organic counterpart naturally embedded astaxanthin, a valuable oxygenated carotenoid with powerful antioxidant properties, which confers attractive advantages compared to the use of geogenic calcium carbonate. These materials are highly abundant and yet little translated to industrial exploitation, although their structure-morphology is the key of developing new drug nanocarriers [2,3] new biostimulants [57,90], efficient pollutant adsorbents [179], pharmaceutical formulations for slow release of active ingredient [2] and many more.

In addressing this research gap, this chapter focuses on the conversion of biogenic calcium carbonate derived from wasted crab carapace into high-value calcium phosphate compounds. The aim of this chapter was twofold: first, to develop and optimize a sustainable chemical and thermal processing route that transforms biogenic calcite into various calcium phosphate phases; and second, to demonstrate that Raman Spectroscopy serves as an effective, real-time, *in situ* analytical tool for monitoring the conversion process.

Raman spectroscopy is an invaluable tool for characterizing calcium phosphate phases due to its sensitivity to subtle differences in molecular vibrations associated with phosphate groups, allowing their identification through characteristic Raman bands. For example, brushite ($CaHPO_4{\cdot}2H_2O$), a hydrated form of calcium hydrogen phosphate, features a prominent band in the region of 985–990 cm^{-1}, which is attributed to the symmetric stretching (ν_1) mode of the HPO_4 group, as well as a weaker band at 875 cm-1 [180]. Monetite ($CaHPO_4$), the anhydrous form of calcium hydrogen phosphate, displays a strong band in the 950–980 cm^{-1} region corresponding to the symmetric stretching vibration of the HPO_4 unit; in some cases, this band exhibits splitting—indicative of subtle structural distortions or heterogeneity—and an additional weaker band at approximately 900 cm^{-1} further distinguishes monetite from brushite [181]. Hydroxylapatite ($Ca_5(PO_4)_3OH$) is characterized by a sharp and intense band near 960 cm^{-1}, corresponding to the symmetric stretching (ν_1) mode of the PO_4^{3-} group; additional bands arising from phosphate bending modes (ν_2 and ν_4) appear around 430–450 cm^{-1} and 580–610 cm^{-1}, while the ν_3 antisymmetric stretching mode is observed between 1000 and 1100 cm^{-1} [182]. Whitlockite ($Ca_9(PO_4)_6(PO_3OH)$) exhibits a main phosphate band slightly shifted to around 968 cm^{-1}, often accompanied by subtle shoulders or additional peaks that reflect the unique local environment of the phosphate groups and may indicate the presence of minor ionic substitutions, such as magnesium [183].

By systematically varying reaction parameters such as acid stoichiometry, particle size, and thermal treatment, the optimal conditions under which the conversion of the biogenic precursor occurs, are explored. In parallel, in situ Raman measurements allow the tracking of the evolution of specific vibrational bands associated with both the starting material and the emerging phosphate phases. This dual focus enhances the practical utility of the final calcium phosphate products, which have wide-ranging applications in fields such as biomedicine, agriculture, water treatment, and food processing.

3.2 Results

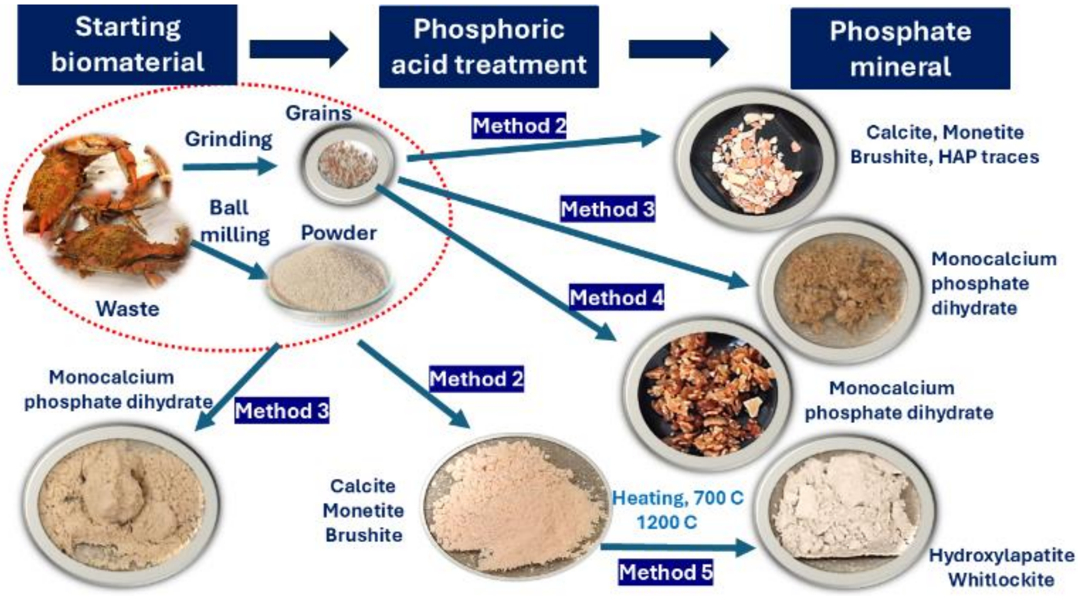


*Figure 3.1 Schematic presentation of the experiments performed on the wasted crustacean shells, along with the reaction products. [**Lazar** et al, 2025, submitted manuscript].*

In this study, we demonstrate the effectiveness of Raman technology in controlling the conversion of biogenic calcite derived from wasted crab shells into calcium phosphate minerals using phosphoric acid treatment. The effects of reaction parameters—including acid stoichiometry, granular size distribution, and thermal treatment at 700°C and 1200°C—were systematically evaluated. Raman spectroscopy validated by X-ray diffraction (XRD) and SEM-EDX analyses revealed mixed-phase minerals monetite, brushite, whitlockite or hydroxylapatite. Notably, reducing particle size enhanced conversion efficiency by increasing the reactive surface area, while the use of excess phosphoric acid facilitated conversion to monocalcium phosphate and promoted the degradation of the organic matrix. Thermal treatment further altered the product composition: heating at 700°C produced a whitlockite-rich phase, whereas treatment at 1200°C shifted the balance toward hydroxylapatite. The synthesized calcium phosphate compounds, including hydroxylapatite, monocalcium phosphate, whitlockite, and brushite hold significant practical utility in biomedical applications (such as bone grafts and dental implants), agriculture, and industrial processing. Moreover, we have proven that by controlling the reaction parameters the final product composition can be tailored according to the specific needs, a greener approach yields brushite, monetite, or monocalcium phosphate while a more energy demanding process including heating to 1200 0C yields a high purity hydroxylapatite.

This research offers a sustainable analytical route for producing high-purity calcium phosphate materials from wasted biomaterials, contributing to both bioeconomy as well as scientific innovation.

Conclusions, impact and perspectives

This thesis highlights the potential of biogenic waste valorization using Raman Spectroscopy, bridging environmental science, biomedical engineering, and pharmaceutical development. It demonstrates that complex biological waste can be repurposed into high-value materials through simple, scalable techniques. The work emphasizes the industrial applicability of these methods, focusing on low-energy processes, cost-effective treatments, and accessible instruments. A key contribution is the use of Raman Spectroscopy to characterize biogenic calcium carbonates and monitor material transformations, such as crystallinity changes, esterification, drug release, and calcium phosphate synthesis. Combined with other techniques like XRD, SEM-EDX, and IR Spectroscopy, Raman offers unmatched versatility for process monitoring and green chemistry.

This research contributes to climate resilience and sustainability by converting biogenic waste, such as crab shells, into valuable materials. The simplicity and scalability of the methods make them adaptable to industrial and resource-limited settings, supporting circular economy models. The novel use of biogenic nanostructures for drug delivery, along with techniques like SERS for compound monitoring, could lead to more effective and eco-friendly therapeutic systems.

The interdisciplinary approach of combining spectroscopy, materials science, and green chemistry offers a blueprint for future research. It contributes to sustainable biomaterials, showing biogenic matrices as versatile precursors for high-value products. Future work will focus on optimizing processes, standardizing methods, and expanding the applications of synthesized materials.

In conclusion, this thesis presents valuable materials, methods, and tools, offering a vision for sustainable innovation in biowaste valorization. By utilizing Raman Spectroscopy, it shows how waste can be transformed into functional materials, driving both scientific understanding and industrial applications. The research embodies circular bioeconomy principles, demonstrating how waste can be converted into valuable resources for various sectors.

List of Publications

Publications on the topic of the thesis

1. Lovro Ogresta, Fran Nekvapil, Tudor Tămaș, Lucian Barbu-Tudoran, Maria Suciu, Răzvan Hirian, Mihaela Aluas, **Geza Lazar**, Erika Levei, Branko Glamuzina, Simona Cintă Pinzaru. Rapid and Application-Tailored Assessment Tool for Biogenic Powders from Crustacean Shell Waste: Fourier Transform-Infrared Spectroscopy Complemented with X-ray Diffraction, Scanning Electron Microscopy, and Nuclear Magnetic Resonance Spectroscopy. *ACS Omega*, vol. 6, no. 42, pp. 27773–27780, 2021, doi: 10.1021/acsomega.1c03279.

Journal name ACS Omega. AIS: 0.63; IF: 4.13, Q2

2. **Geza Lazar**, Fran Nekvapil, Razvan Hirian, Branko Glamuzina, Tudor Tamas, Lucian Barbu-Tudoran, Simona Cinta Pinzaru. "Novel drug carrier: 5-Fluorouracil formulation in nanoporous biogenic Mg-calcite from blue crab shells—Proof of concept" *ACS Omega*, vol. 6, no. 42, pp. 27781–27790, 2021, doi: 10.1021/acsomega.1c03285.

Journal name ACS Omega. AIS: 0.63; IF: 4.13, Q2

3. **Geza Lazar**, Fran Nekvapil, Sanja Matić-Skoko, Călin Firta, Dario Vrdoljak, Hana Uvanović, Lucian Barbu-Tudoran, Maria Suciu, Luka Glamuzina, Branko Glamuzina, Regina Mertz-Kraus, Simona Cinta Pinzaru. "Comparative screening the life-time composition and crystallinity variation in gilthead seabream otoliths Sparus aurata from different marine environments," Sci. Rep., vol. 12, p. 9584, 2022, doi: 10.1038/s41598-022-13667-3.

Journal name Scientific reports. AIS: 1.132; IF: 4.60, Q1

4. **Geza Lazar**, Fran Nekvapil, Branko Glamuzina, Tudor Tamaș, Lucian Barbu-Tudoran, Maria Suciu, Simona Cinta Pinzaru. ''pH-Dependent Behavior of Novel 5-FU Delivery System in Environmental Conditions Comparable to the Gastro-Intestinal Tract" *Pharmaceutics*, vol. 15, p. 1011, 2023, doi: 10.3390/pharmaceutics15031011.

Journal name Pharmaceutics. AIS: 0.798; IF: 4.9, Q1

5. Cristina Adriana Dehelean, Dorina Coricovac, Iulia Pinzaru, Iasmina Marcovici, Ioana Gabriela Macasoi, Alexandra Semenescu, **Geza Lazar**, Simona Cinta Pinzaru, Isidora Radulov, Ersilia Alexa, Octavian Cretu. "Rutin bioconjugates as potential nutraceutical prodrugs: An in vitro and in ovo toxicological screening," *Front. Pharmacol.*, vol. 13, 2022, doi: 10.3389/fphar.2022.1000608.

Journal name Frontiers in Pharmacology. AIS: 0.995; IF: 5.60, Q1

6. Cristina Dehelean, Ersilia Alexa, Iasmina Marcovici, Andrada Iftode, **Geza Lazar**, Andrea Simion, Vasile Chis, Adrian Pirnau, Simona Cinta Pinzaru, Estera Boeriu. "Synthesis, Characterization, and in vitro–in Ovo Toxicological Screening of Silibinin Fatty Acids Conjugates As Prodrugs With Potential Biomedical Applications," *Biomolecules and Biomedicine*, vol. 24, no. 6, pp. 1735–1750, 2024, doi: 10.17305/bb.2024.10600.

Journal name Biomolecules and Biomedicine. N/A

7. Fran Nekvapil, Maria Mihet, **Geza Lazar**, Simona Cîntă Pinzaru, Ana Gavrilović, Alexandra Ciorîță, Erika Levei, Tudor Tamaș, Maria-Loredana Soran Composition and Porosity of the Biogenic Powder Obtained from Wasted Crustacean Exoskeletonsafter Carotenoids Extraction for the Blue Bioeconomy. *Water*, 15, 2591. https://doi.org/10.3390/w15142591

Journal name: Water. AIS: 0.528; IF: 3.0, Q2

8. **SUBMITED MANUSCRIPT**: **Geza Lazar,** Tudor Tămaş, Lucian Barbu-Tudoran, Monica M. Venter, Ilirjana Bajama, and Simona Cintă Pinzaru. Biowaste valorisation: Conversion of Crab Shell-Derived Mg-Calcite into Calcium Phosphate Minerals Controlled by Raman Spectroscopy. Submitted to Biomaterials Science.

Journal name: Journal of Materials Science. AIS: 0.666; IF: 3.9, Q2

9. **SUBMITED MANUSCRIPT**: Ilirjana Bajama, Karlo Maškarić, Geza Lazar, Tudor Tămaș, Codrut Costinas, Lucian Barbu-Tudoran, Simona Cîntă Pînzaru. Years-aged biogenic carbonates from crustacean waste: struc-tural and functional evaluation of calibrated fine powders and their conversion into phosphate minerals.

Journal name: Materials. AIS: 0.523; IF: 3.2, Q3

7 publications included in the thesis: total AIS = 4.713. 3 Q1; 3 Q2; 1 N/A

Other publications

1. **Geza Lazar**, Calin Firta, Sanja Matić-Skoko, Melita Peharda, Dario Vrdoljak, Hana Uvanović, Fran Nekvapil, Branko Glamuzina, S CintaPinzaru. 'Tracking the growing rings in biogenic aragonite from fish otolith using confocal raman microspectroscopy and imaging'. *Studia UBB Chemia*, 65(1), 125–136. https://doi.org/10.24193/subbchem.2020.1.10.

Journal name: Studia Chemia. AIS: 0.0.062; IF: 0.46, Q4

2. Fran Nekvapil, Ioana Brezestean, **Geza Lazar**, Calin Firta, Simona Cinta Pinzaru. Resonance Raman and SERRS of fucoxanthin: Prospects for carotenoid quantification in live diatom cells. *J. Mol. Struct.* **2021**, *1250*, 131608. https://doi.org/10.1016/j.molstruc.2021.131608.

Journal name: Journal of Molecular Structure. AIS: 0.385; IF: 3.8, Q2

9 publications in total: total AIS = 5.16. 46 citations, H-index 5 (Scopus, WoS, Google scholar).

Conference Contributions

1. Geza Lazar, Fran Nekvapil, Razvan Hirian, Branko Glamuzina, Tudor Tamaș, Lucian Barbu-Tudoran and Simona Cinta Pinzaru. *PH dependent fluorouracil release from novel composite drug based on biogenic calcium carbonate*. Poster: ICPAM 14, Dubrovnik, Croatia 7-16 Septembrer 2022.

2. Effects of ocean acidification on the morphology and structure of Hexaplex trunculus sea snail shell biomaterial revealed by Raman, XRD AND SEM-EDX data. **G. Lazar**, F. Nekvapil, I. Bajama, T. Tamas, M. Suciu, L. BarbuTodoran, S. Grdan, S. Cinta Pinzaru, S. Dupont, A. Bratos Cetinic, L. Glamuzina. Oral presentation: ICPAM 14, Dubrovnik, Croatia 7-16 Septembrer 2022.

3. New biocomposites from waste materials S. Cinta Pinzaru, **G. Lazar**, F. Nekvapil, R. Hirian, T. Tamas, L. Barbu-Tudoran, M. Suciu, M. Aluas, I. Bajama, D. A. Dumitru, S. Tomsic, B. Glamuzina. . ICPAM 14, Dubrovnik, Croatia 7-16 Septembrer 2022.

4. Screening of waste shell biomaterials for recycling as adsorbents for water-borne pollutants. F. Nekvapil, **G. Lazar**, M-L. Soran, M. Mihet, R. Hirian, A. Ciorita, S.B. Angyus, T. Kusovaca, M. Precanica, S. Cinta Pinzaru. ICPAM 14, Dubrovnik, Croatia 7-16 Septembrer 2022.

5. Doxycycline hyclate loaded in porous biogenic carbonate: new drug formulation and characterization using Raman spectroscopy techniques and XRD. I. Bajama, **G. Lazar**, T. Tamas, S. Cinta Pinzaru. ICPAM 14, Dubrovnik, Croatia 7-16 Septembrer 2022.

6. Multiplexed SERS for wastewater treatment utilizing highly absorbent biogenic powders to eliminate environmentally realistic mixtures comprising inorganic pollutants. Ilirjana Bajama, **Geza Lazar**, Tudor-Liviu Tamas, Simona Cinta Pinzaru. Poster: ICORS 2024, Rome, Italy 28 July - 2 August 2024.

7. Raman technology for the development of a novel biogenic calcite based bone substitute material. **Geza Lazar**, Ilirjana Bajama, Tudor Tamas, Simona Pinzaru. Accepted abstract. Poster: ICORS 2024. Rome, Italy 28 July - 2 August 2024.

8. Chemical structure, morphology and bioeconomy of the biogenic material derived from the invasive gastropod Rapana venosa shell by multi-laser Raman, XRD and SEM-EDX. D-Al. Dumitru, **G. Lazar**, F. Nekvapil, T. Tamas, L. BarbuTudoran, S. Cinta Pinzaru. ICPAM 14, Dubrovnik, Croatia 7-16 Septembrer 2022.

9. Innovative biofertilizer from two aquatic waste materials and its influence on carotenoid content in lettuce crop F. Nekvapil, G. Lazar, R. Hirian, M. Aluas, M. Suciu, T. Tamas, L. Barbu-Tudoran, S. Tomsic, B. Glamuzina, S. Cinta Pinzaru. . ICPAM 14, Dubrovnik, Croatia 7-16 Septembrer 2022.

10. New Drug Carrier for Slow Release: 5-Fluorouracil Formulation in Nanoporous Biogenic Mg-calcite from Blue Crab Shell. **Geza Lazar**, Fran Nekvapil, Razvan Hirian, Branko Glamuzina, Tudor Tamaș, Lucian Barbu-Tudoran, Maria Suciu Simona Cinta Pinzaru. Poster: PIM 2021, 22-24 September 2021, Cluj-Napoca.

Other Activities

Second Workshop on Blue Bioeconomy Approach to Marine Biomass Waste: INNOVATIVE IDEAS, TECHNIQUES AND TRANSLATIONAL SCIENCES. Oral Presentation: **Geza Lazar**, Novel drug carrier from biogenic calcite popwder from crustaceans. 20 October 2021, Dubrovnik Croatia.

Attendance Summer School Microplastics: From Environmental Impact to Policy, Innovation, and Public Awareness,16-20 June 2025, Geneve, Switzerland.

Research Project: BlueBioSustain From Nanobiosensing to Blue Bioeconomy:Translational Science as Innovation Speeder of Blue Growth.

PROJECT: PN-III-P2-2.1-PED-2019-4777.
https://bluebiosustain.granturi.ubbcluj.ro/

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