# AAP China Scholarship Council - CSC 2023

# PROJET DE RECHERCHE DOCTORALE (PRD)

**Titre du PRD : Oral controlled delivery with agromaterials (chitosan and soy proteins isolates)**

## DIRECTION de THESE

**Porteuse ou porteur du projet** (***doit être titulaire de l'HDR***) :


**NOM : CASTIGNOLLES**

Prénom : Patrice

Titre : PU ou Autre :

Section CNU : 33

Email : patrice.castignolles@sorbonne-universite.fr

Unité de recherche : Code (ex. UMR xxx) et Intitulé : UMR8232, Institut Parisien de Chimie Moléculaire (IPCM)

Ecole doctorale de rattachement : ED397 - Physique et Chimie des Matériaux

Nombre de doctorants actuellement encadrés : 2


## CO-DIRECTION de THESE (HDR) ou CO-ENCADREMENT (Non HDR) :


**NOM :**

Prénom :

Titre : Sélectionner ou Autre :

Section CNU : D

Email :

Unité de recherche : Code (ex. UMR xxx) et Intitulé :

Ecole doctorale de rattachement : Sélectionner

Nombre de doctorants actuellement encadrés :

**CO-TUTELLE INTERNATIONALE envisagée : ☐ OUI ☒ NON**

## DESCRIPTIF du PRD :

*Ce texte sera affiché en ligne à destination des candidates et candidats chinois : il ne doit pas excéder **2 pages** doit être rédigé en **ANGLAIS***

1) Study context

Agromaterials are materials obtained from agriculture waste. They are biobased. Two polymers are particularly of interest for medical research: chitosan and soy protein isolates. Chitosan is obtained from the chitin of crab or prawn shell. It is an important waste from the seafood industry. It also has valuable properties on top of being biobased: bacteriostaticity, biocompatibility, pH-responsivity. Soy proteins isolates are a left-over from tofu production. They are biocompate but also not soluble in common solvents. This makes them particularly relevant for oral delivery of painkillers, vitamins and drugs.

Oral delivery is sought for obvious advantages for the user: no injection. However, oral delivery presents a challenge in the excipient design. The capsule with the drug, painkiller or vitamin needs to be inert in the acidic conditions of the stomach but to lead to a quick delivery later on in the intestine. Both chitosan and soy proteins isolates are good candidates for oral delivery. Chemical modification allows adjusting their properties.[1] We have started with the painkiller ibuprofen[2] and with vitamins as first candidates for encapsulation with (chemically-modified) chitosan and soy proteins isolates. The encapsulation is done by spray-drying, a method mastered by our collaborators at Toulouse Institut National Polytechnique, France [3].

2) Details of the proposal

Some chitosans, soy proteins isolates, chemically modified or not, are already available for the project as well as capsules of ibuprofen or vitamins obtained with these polymers. Additional capsules can be produced to improve drug loading, resistance to gastric conditions or release in intestinal conditions.

The molar size (hydrodynanic radius), molar mass and chemical composition of chitosan and soy proteins samples, before and after chemical modification, will be determined using size-exclusion chromatography (SEC, also known as GPC) [4] as well as NMR spectroscopy and capillary electrophoresis [5]. The capsules will be characterized in terms of chemical composition using conventional spectroscopy methods such as FT-IR and more advanced ones when needed such as solid-state NMR.[6] Their morphology will be characterized using electron microscopy, typically scanning electron microscopy (SEM).

Gastric fluid and intestinal fluid, as defined by pharmacopea, will be used to simulate conditions in the stomach and small intestine respectively. The solubility of the polymers and capsules will be first tested using turbidity measurements as well as solution-state NMR and capillary electrophoresis ones.[7] Capsules soluble in gastric fluid will not be further used. The delivery from the remaining capsules will be monitored using high-performance liquid chromatography (HPLC), NMR spectroscopy and capillary electrophoresis. The impact of the presence or absence of food in the gastric and intestinal fluid will be investigated. Capillary electrophoresis will be especially relevant for this due to the robustness of this method.[7-8]

Structure-property relations will be established. In terms of structure, the size and chemical composition of the chitosan and soy proteins isolates, their chemical composition after chemical modification, the morphology and size of the capsules will be considered. The properties of interest

include no solubility (or even release) in gastric fluid, and quick release in intestinal fluid. New polymers will be sourced, new chemical modifications will be performed and new capsules fabricated. The structure of the polymers (molar mass, chemical compostions), conditions for chemical modifications (nature of the agent, stoichiometry, temperature, etc.) and capsule formation will be adjusted to improve the properties. The properties of the new capsules will then be determined.

3) References

[1] Nesterenko, A., Alric, I., Violleau, F., Silvestre, F., & Durrieu, V. (2014). The effect of vegetable protein modifications on the microencapsulation process. Food Hydrocolloids, 41, 95-102.

[2] Castro, M. A. A., Alric, I., Brouillet, F., Peydecastaing, J., Fullana, S. G., & Durrieu, V. (2019). Spray-Dried Succinylated Soy Protein Microparticles for Oral Ibuprofen Delivery. Aaps Pharmscitech, 20(2), 10.

[3] Choque, E., Durrieu, V., Alric, I., Raynal, J., & Mathieu, F. (2019). Impact of Spray-Drying on Biological Properties of Chitosan Matrices Supplemented with Antioxidant Fungal Extracts for Wine Applications. Current Microbiology, 10, 210-219.

[4] Gaborieau, M., & Castignolles, P. (2011). Size-exclusion chromatography (SEC) of branched polymers and polysaccharides. Analytical and Bioanalytical Chemistry, 399, 1413-1423.

[5] Thevarajah, J. J., Van Leeuwen, M. P., Cottet, H., Castignolles, P., & Gaborieau, M. (2017). Determination of the distributions of degrees of acetylation of chitosan. International Journal of Biological Macromolecules, 95, 40-48.

[6] Bhullar, K. A., Horgan, M. I. M., Le, A., Fania, D., Wuhrer, R., Razmovski-Naumovski, V., Chan, K., Castignolles, P., & Gaborieau, M. (2022). Assessing the quantification of acetylation in konjac glucomannan via ATR-FTIR and solid-state NMR spectroscopy. Carbohydrate Polymers, 291, 119659.

[7] Thevarajah, J. J., Bulanadi, J. C., Wagner, M., Gaborieau, M., & Castignolles, P. (2016). Towards a less biased dissolution of chitosan. Analytica Chimica Acta, 935, 258-268.

[8] Oliver, J. D., Sutton, A. T., Karu, N., Phillips, M., Markham, J., Peiris, P., Hilder, E.F., & Castignolles, P. (2015). Simple and robust monitoring of ethanol fermentations by capillary electrophoresis. Biotechnology and Applied Biochemistry, 62(3), 329-342.

4°) Profile of the Applicant (skills/diploma…)

We are looking for a motivated candidate with practical experience in polymer science or analytical chemistry.

**AVIS de l'Ecole Doctorale :**

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**NOM Prénom_Projet CSC 2023.pdf**

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**à l'école doctorale de rattachement et à csc-su@listes.upmc.fr**