Peptidyl-proline isomerase (PPIases) are a chaperone superfamily comprising the FK506-binding proteins (FKBPs), cyclophilins, and parvulins. PPIases catalyze the cis/trans isomerization of proline, acting as a regulatory switch during folding, activation, and/or degradation of many proteins. These "clients" include proteins with key roles in cancer, neurodegeneration, and psychiatric disorders, suggesting that PPIase inhibitors could be important therapeutics. However, the active site of PPIases is shallow, solvent-exposed, and well conserved between family members, making selective inhibitor design challenging. Despite these hurdles, macrocyclic natural products, including FK506, rapamycin, and cyclosporin, bind PPIases with nanomolar or better affinity. De novo attempts to derive new classes of inhibitors have been somewhat less successful, often showcasing the "undruggable" features of PPIases. Interestingly, the most potent of these next-generation molecules tend to integrate features of the natural products, including macrocyclization or proline mimicry strategies. Here, we review recent developments and ongoing challenges in the inhibition of PPIases, with a focus on how natural products might inform the creation of potent and selective inhibitors. [Dunyak, B.M. and Gestwicki, J.E*. (Department of Pharmaceutical Chemistry, University of California at San Francisco, 675 Nelson Rising Lane, San Francisco, CA, United States), Journal of Medicinal Chemistry, 2016, 59(21), 9622-9644].

Microcapsules derived from plant-based spores or pollen provide a robust platform for a diverse range of microencapsulation applications. Sporopollenin exine capsules (SECs) are obtained when spores or pollen are processed so as to remove the internal sporoplasmic contents. The resulting hollow microcapsules exhibit a high degree of micromeritic uniformity and retain intricate microstructural features related to the particular plant species. Herein, we demonstrate a streamlined process for the production of SECs from Lycopodium clavatum spores and for the loading of hydrophilic compounds into these SECs. The current SEC isolation procedure has been recently optimized to significantly reduce the processing requirements which are conventionally used in SEC isolation, and to ensure the production of intact microcapsules. Natural L. clavatum spores are defatted with acetone, treated with phosphoric acid, and extensively washed to remove sporoplasmic contents. After acetone defatting, a single processing step using 85% phosphoric acid has been shown to remove all sporoplasmic contents. By limiting the acid processing time to 30 hr, it is possible to isolate clean SECs and avoid SEC fracturing, which has been shown to occur with prolonged processing time. Extensive washing with water, dilute acids, dilute bases, and solvents ensures that all sporoplasmic material and chemical residues are adequately removed. The vacuum loading technique is utilized to load a model protein (Bovine Serum Albumin) as a representative hydrophilic compound. Vacuum loading provides a simple technique to load various compounds without the need for harsh solvents or undesirable chemicals which are often required in other microencapsulation protocols. Based on these isolation and loading protocols, SECs provide a promising material for use in a diverse range of microencapsulation applications, such as, therapeutics, foods, cosmetics, and personal care products [Potroz, M.G., Mundargi, R.C., Park, J.H., Tan, E.L. and Cho, N.-J*(School of Materials Science and Engineering, Nanyang Technological University, Singapore), Journal of Visualized Experiments, 2016, 2016(117), 54768].
Development of novel HER2 inhibitors against gastric cancer derived from flavonoid source of *Syzygium alternifolium* through molecular dynamics and pharmacophore-based screening

Continuous usage of synthetic chemotherapeutic drugs causes adverse effects, which prompted for the development of alternative therapeutics for gastric cancer from natural source. This study was carried out with a specific aim to screen gastroprotective compounds from the fruits of *Syzygium alternifolium* (Myrtaceae). Three flavonoids, namely, 1) 5-hydroxy-7,4′-dimethoxy-6,8-di-C-methylflavone, 2) kaempferol-3-O-β-d-glucopyranoside, and 3) kaempferol-3-O-α-l-rhamnopyranoside were isolated from the above medicinal plant by employing silica gel column chromatography and are characterized by NMR techniques. Antigastric cancer activity of these flavonoids was examined on AGS cell lines followed by cell cycle progression assay. In addition, pharmacophore-based screening and molecular dynamics of protein–ligand complex were carried out to identify potent scaffolds. The results showed that compounds 2 and 3 exhibited significant cytotoxic effect, whereas compound 1 showed moderate effect on AGS cells by inhibiting G2/M phase of cell cycle. Molecular docking analysis revealed that compound 2 has higher binding energies on human growth factor receptor-2 (HER2). The constructed pharmacophore models reveal that the compounds have more number of H-bond Acc/Don features which contribute to the inhibition of HER2 activity. By selecting these features, 34 hits were retrieved using the query compound 2. Molecular dynamic simulations (MDS) of protein–ligand complexes demonstrated conspicuous inhibition of HER2 as evidenced by dynamic trajectory analysis. Based on these results, the compound ZINC67903192 was identified as promising HER2 inhibitor against gastric cancer. The present work provides a basis for the discovery a new class of scaffolds from natural products for gastric carcinoma [Babu, T.M.C., Rammohan, A., Baki, V.B., Devi, S., Gunasekar, D. and Rajendra, W*. (Bioinformatics Center, Division of Molecular Biology, Department of Zoology, Sri Venkateswara University, Tirupati, Andhra Pradesh, India), *Drug Design, Development and Therapy*, 2016, 10, 3611-3632].

Screening for marine natural products with potential as chemotherapeutics for acute myeloid Leukemia

Nature is an important source for anti-cancer therapeutics, and nearly half of the currently marketed cancer drugs are derived from natural products. Most of the therapeutic natural products are derived from terrestrial sources, such as paclitaxel, vincristine, epothilones, doxorubicin, etoposide and camptothecin. However, the oceans have received growing interest as a source for new useful bioactive compounds, and there are currently several drugs derived from marine natural products for the treatment of cancer on the market. The current recommended chemotherapy of acute myeloid leukemia (AML) is founded on cytarabine, a molecule derived from a natural product isolated from a marine sponge. However, in order to increase the efficiency of the chemotherapy used in the treatment of AML, it is necessary to develop more targeted drugs with less pronounced side effects. In this review, we argue that marine natural products have many of the desired properties of such a drug, and that prefractionated extract libraries of marine plants, animals and microorganisms should be a part of the screening efforts for new AML chemotherapeutics [Hansen, E. and Andersen, J.H*. (UiT The Arctic University of Norway, Norway), *Current Pharmaceutical Biotechnology*, 2016, 17(1), 71-77].

Recent developments in chimeric NSAIDs as anticancer agents: Teaching an old dog a new trick

Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the widely used medications all over the world, indicated for pain, fever, and
inflammation. It is now well established that inflammation and cancer are closely linked with each other. Inflammatory mediators, like cyclooxygenase (COX), vascular endothelial growth factor (VEGF), tumor growth factor (TGF), fibroblast growth factor (FGF), chemokines, and cytokines and related genes, such as inhibitor of nuclear factor-kappa B kinase (IKK) and nuclear factor-kappa B (NF-κB) have been shown to be up-regulated in various cancers. Till date, numerous anticancer agents of different classes have been discovered to treat and eradicate various forms of cancer; though, limitations like cytotoxicity to normal cells and acquired tumor resistance restrict the scope of present cancer therapeutics. NSAIDs have shown to decrease the incidence, recurrence, and proliferation of various cancers, viz. colon, breast, lung, and pancreatic, etc. Therefore, the developing agents, such as NO-and H$_2$S-releasing NSAIDs, NSAID-metal complexes, natural product-NSAID conjugates, phospho-NSAIDs, and various other NSAIDs derivatives represent the next generation therapeutics to treat both inflammation and cancer [Suthar, S.K. and Sharma, M.*. (Department of Pharmaceutical Chemistry, M.M. University, Mullana, Distt, Ambala, India), *Mini-Reviews in Medicinal Chemistry*, 2016, *16*(15), 1201-1218].

*NPARR, 8(1), 2017-189* **Overview of biopolymers as carriers of antiphlogistic agents for treatment of diverse ocular inflammations**

Inflammation of the eye is a usual clinical condition that can implicate any part of the eye. The nomenclature of variety of such inflammations is based on the ocular part involved. These diseases may jeopardize normal functioning of the eye on progression. In general, corticosteroids, antihistamines, mast cell stabilizers and non-steroidal anti-inflammatory drugs (NSAIDs) are used to treat inflammatory diseases/disorders of the eye. There have been several attempts via different approaches of drug delivery to overcome the low ocular bioavailability resulting from shorter ocular residence time. The features like safety, ease of elimination and ability to sustain drug release have led to application of biopolymers in ocular therapeutics. Numerous polymers of natural origin such as gelatin, collagen, chitosan, albumin, hyaluronic acid, alginites etc. have been successfully employed for preparation of different ocular dosage forms. Chitosan is the most explored biopolymer amongst natural biopolymers because of its inherent characteristics. The emergence of synthetic biopolymers (like PVP, PACA, PCL, POE, polyanhydrides, PLA, PGA and PLGA) has also added new dimensions to the drug delivery strategies meant for treatment of ophthalmic inflammations. The current review is an endeavor to describe the utility of a variety of biomaterials/polymers based drug delivery systems as carrier for anti-inflammatory drugs in ophthalmic therapeutics [Sharma, A.K.*, Arya, A., Sahoo, P.K. and Majumdar, D.K. (Delhi Institute of Pharmaceutical Sciences and Research, Formerly College of Pharmacy, University of Delhi, Pushp Vihar, Sector III, New Delhi, India), *Materials Science and Engineering C*, 2016, *67*, 779-791].

*NPARR, 8(1), 2017-190* **Gastrodia elata and epilepsy: Rationale and therapeutic potential**

Background: *Gastrodia elata* Blume (*G. elata*) is a traditional Chinese herb used for centuries in folk medicine. Due to the claimed anticonvulsant properties of *G. elata*, it is expected that this herb continues to be a target of research, aiming to deepen the available knowledge on its biological activity and safety. Purpose: The current review aims to discuss the most recent advances on the elucidation of the phytochemical composition and anticonvulsant potential of *G. elata*. Methods Available literature was reviewed from PubMed, ISI Web of Knowledge and Science Direct, using combinations of the following keywords:
Gastrodia elata, tianma, epilepsy, anticonvulsant and pharmacokinetics. Abstracts and full texts were evaluated for their clarity and scientific merit. Results: G. elata rhizome, as well as specific phenolic compounds isolated from this herb, has demonstrated anticonvulsant potential in a variety of in vitro and in vivo models. The pharmacological mechanisms potentially involved in the anticonvulsant activity have been extensively studied, being similar to the known mechanisms claimed for the available antiepileptic drugs. In addition, the pharmacokinetics of the main bioactive component of G. elata (gastrodin) has also been studied. Conclusion: Due to its recognised therapeutic properties, G. elata has gained an increasing interest within the scientific community and, therefore, new medicinal preparations containing G. elata rhizome itself or its bioactive components are expected to be developed in the coming years. Moreover, specific phytochemical constituents isolated from G. elata may also be considered to integrate programs of discovery and development of new anticonvulsant drug candidates [Matias, M., Silvestre, S., Falcão, A. and Alves, G*. (CICS-UBI – Health Sciences Research Centre, University of Beira Interior, Rua Marquês d’Ávila e Bolama, Covilhã, Portugal), Phytomedicine, 2016, 23(12), 1511-1526].

NPARR, 8(1), 2017-191 Development of a plant based confectionary to combat micro-sleepiness due to fatigue in hectic life-styles and cerebral relaxation

Background: Micro-sleepiness (MS) is a temporary biological disorder, which can lasts from fraction of second to 30 sec and an individual fails to respond for some arbitrary sensory inputs. It has become one of the major social issues that cause fatalities, material losses, productivity and quality dilapidation and eventually negative impact on national GDP. Methodology: To combat this adverse biological phenomenon, plant based phytochemicals in berries of Piper nigrum, beans of Coffea arabica, bark of Cinnamomum verum and rhizomes of Zingiber officinale were extracted and incorporated to develop an effective confectionary. Boosting the self-confident level, mortar function, gustatory stung action, astonish olfactory and tingling actions and chemical energy were impregnated into the confection using aforesaid raw materials to combat MS. Series of confectionaries were developed based on advanced Thaguchi statistical design and best treatment was selected organoleptically against five sensory stimuli: Color, taste, mouth feel, texture, odour and overall acceptability. Results: Results revealed mean deviations of above sensory attributes were 3.85±0.81, 3.65±0.58, 3.6±0.94, 3.55±0.94, 3.45±0.76 and 3.75±0.55, respectively. Piperine, caffeine, cinnamaldehyde and gingerol were at 12.727, 5.277, 1.333 and 0.533 mg, respectively in the developed product and below the WHO standards. The developed product was capable to suppress MS completely, controlled at a satisfactory level and fails to control for 15, 65 and 15%, respectively. Further 35, 30, 20 and 15% expressed that they didn't feel MS 1-2, <1, 2-3, 3-4 h respectively. Conclusion: Thus the developed product was capable to combat MS in modern busy life styles without any adverse effects or allergies [Liyanage, R*, Navaratne, S.B., Wickramasinghe, I. and Ranaweera, K.K.D.S. (Department of Food Science and Technology, Faculty of Applied Sciences, University of Sri Jayewardenepura, Gangodawlla, Nuageoda, Sri Lanka), Pakistan Journal of Nutrition, 2016, 15(12), 1017-1025].

NPARR, 8(1), 2017-192 Hypolipidemic and antioxidant properties of hot pepper flower (Capsicum annuum L.)

At present, the various medical treatments of obesity involve side effects. The aim of the research is therefore to find natural compounds that have anti-obesity activity with minimum disadvantages. In this study, the hypolipidemic effect of hydroalcoholic extract of
flowers from *Capsicum annuum* L. was examined through the evaluation of inhibition of pancreatic lipase. Antioxidant activity was assessed using different tests: 2,2-diphenyl-1-picrylhydrazyl (DPPH), nitric oxide (\(\dot{\text{NO}}\)) and lipid peroxidation inhibition assays. Phytochemical analysis indicated that total phenolic and flavonoid content in the extract was 128.7 ± 4.5 mg chlorogenic acid equivalent/g of crude extract and 17.66 ± 0.11 mg of quercetin equivalent/g of crude extract, respectively. The extract inhibited pancreatic lipase with IC\(_{50}\) value equal to 3.54 ± 0.18 mg/ml. It also inhibited lipid peroxidation with IC\(_{50}\) value of 27.61 ± 2.25 µg/ml after 30 min of incubation and 41.69 ± 1.13 µg/ml after 60 min of incubation. The IC\(_{50}\) value of radical scavenging activity was 51.90 ± 2.03 µg/ml. The extract was also able to inhibit NO production (IC\(_{50}\) = of 264.3 ± 7.98 µg/ml) without showing any cytotoxic effect [Marrelli, M., Menichini, F. and Conforti, F*. (Department of Pharmacy, Health and Nutritional Sciences, University of Calabria, Rende, (CS), Italy), *Plant Foods for Human Nutrition*, 2016, **71**(3), 301-306].

NPARR, 8(1), 2017-193 Ameliorative and antioxidant effects of myrtle berry seed (*Myrtus communis*) extract during reflux-induced esophagitis in rats

Context *Myrtle, Myrtus communis* L. (Myrtaceae), is a medicinal plant well known for its richness in phenolic compounds and its beneficial effects for the treatment of gastrointestinal disorders. Objective: In the present work, the protective effect of the myrtle berry seed aqueous extract (MBSAE) against esophageal reflux (ER)-induced damage in esophagus mucosa as well as the mechanisms implicated was determined. Materials and methods: In this respect, adult male Wistar rats were used and divided into seven groups: Control, ER, ER + various doses of MBSAE, ER + famotidine or ER + gallic acid. The ER was induced and animals were per orally (p.o.) treated with MBSAE or reference molecules during 6 h. The phytochemical screening was determined using colourimetric analysis. Results: MBSAE is rich in total polyphenols and anthocyanins and exhibited an important *in vitro* antioxidant activity. *In vivo*, we firstly found that ER led to marked macroscopic and histopathological changes in esophagus. The results showed, also, that the ER was accompanied by a state of oxidative stress as assessed by an increase of lipid peroxidation, a decrease of the sulphydryl groups and glutathione levels, as well as antioxidant enzyme activities depletion. MBSAE abrogated all morphological, histopathological and biochemical alterations. We showed also that ER increased esophageal calcium, hydrogen peroxide (H\(_2\)O\(_2\)) and free iron levels while MBSAE treatment protected against intracellular mediators deregulation. Conclusion: Our data suggest that MBSAE exerted a potential protective effect against ER-induced damage in rat esophagus, at least in part, due to its antioxidant properties [Jabri, M.A., Tounsi, H., Rtibi, K., Marzouki, L., Sakly, M. and Sebai, H*. (Laboratoire De Physiologie Intégrée, Faculté Des Sciences De Bizerte, Zarzouma, Tunisia), *Pharmaceutical Biology*, 2016, **54**(9), 1575-1585].

NPARR, 8(1), 2017-194 Cytotoxic and antimalarial constituents from aerial parts of *Sphaeranthus indicus*

Two new eudesmanolide type sesquiterpenes, indicusalactone (1) and (−)-oxyfrullanolide (2), along with twelve known compounds (3–14), were isolated from the aerial parts of *Sphaeranthus indicus*. The structures of these compounds were established on the basis of their 1D and 2D NMR spectroscopic data. Compounds 1–4 and 12–14 showed antimalarial activity against *Plasmodium falciparum* with IC\(_{50}\) values ranging from 2.32 to 6.47 µg/mL. In addition, compounds 2–5 showed cytotoxicity against cancer cell lines, KB, NCI-H187 and MCF-7 with IC\(_{50}\) values within the range 1.23–46.19 µg/mL [Sangsopha, W., Lekphrom, R*, Kanokmedhakul, S. and Kanokmedhakul, K. (Natural Products Research Unit, Department of
Chemistry and Center for Innovation in Chemistry, Faculty of Science, Khon Kaen University, Khon Kaen, Thailand), *Phytochemistry Letters*, 2016, **17**, 278-281].

*NPARR*, 8(1), 2017-195 **Chemical characterization and bioactive properties of aqueous and organic extracts of *Geranium robertianum* L.**

*Geranium robertianum* L. has been used in folk medicine and herbalism practice for the treatment of various conditions, but the study of its bioactivity has been barely addressed. Although its phytochemical composition has received some attention, contributions to the nutritional composition are practically unknown. Herein, *G. robertianum* gathered in Trás-os-Montes, Northeastern Portugal, was chemically characterized regarding nutritional parameters, and the antioxidant activity and cytotoxicity against several human tumor cell lines and non-tumor porcine liver primary cells of several aqueous and organic extracts were evaluated. *G. robertianum* showed to be an equilibrated valuable herb, rich in carbohydrates and proteins, and poor in fat, providing sugars, tocopherols, organic and essential fatty acids. Amongst the extracts, the acetone one showed the highest total phenol and total flavonoid contents, as well as the greatest antioxidant and cytotoxic activities. This extract showed to contain hydrolysable tannins (e.g. geraniin and castalagin/vescalagin), as the main phenolic compounds [Graça, V.C., Barros, L., Calhelha, R.C., Dias, M.L., Carvalho, A.M., Santos-Buelga, C., Santos, P.F. and Ferreira, I.C.F.R*. (Mountain Research Centre (CIMO), ESA, Polytechnic Institute of Bragança, Campus de Santa Apolónia, 1172, Bragança, Portugal), *Food and Function*, 2016, 7(9), 3807-3814]

*NPARR*, 8(1), 2017-196 **In vitro bioactivity and antimicrobial activity of Picea abies and Larix decidua wood and bark extracts**

*Picea abies* and *Larix decidua* were subjected to GC/MS analyses, and antimicrobial (fungi and bacteria) assays of their stem wood and bark extracts were investigated. *L. decidua* bark extract exhibited the highest antifungal and antibacterial activities against the microorganisms that were screened. The microbes *Penicillium ochrochloron* and *Aspergillus ochraceus* were the most sensitive to the extracts, whereas *Candida albicans* was the most resistant fungus. *L. decidua* wood and bark did not exhibit much variation in their antibacterial activities, except against *Micrococcus flavus* and *Pseudomonas aeruginosa*. The bacterium most sensitive to the extracts was *Escherichia coli*, whereas the most resistant was *M. flavus*. 13-epimanool and α-cedrol were the main components of *P. abies* wood extract. The main components in its bark were abietic acid, astringin, dehydroabiatic acid, and α-terpineol. The main chemical compounds in *L. decidua* wood extract were abietic acid, oleanolic acid, duvatrienediol, and larixol. The main chemical compounds in its bark were (-)-2,9-dihydroxyverrucosane and larixol. The study revealed that *P. abies* and *L. decidua* stem wood and bark extracts contain several compounds that have antimicrobial activities towards diverse human pathogenic, food, and agricultural microbes. These results might guide in future searches for novel natural products with chemotherapeutic uses [Salem, M.Z.M.*, Elansary, H.O., Elkelish, A.A., Zeidler, A., Ali, H.M., Hefny, M.E.L. and Yessoufou, K. (Department of Forestry and Wood Technology, Faculty of Agriculture (El-Shatby), Alexandria University, Alexandria, Egypt), *BioResources*, 2016, 11(4), 9421-9437].