Production of anti-prostate cancer Myrrhanol C

Priority: July 2012.

Features: The invention describes the synthesis of a myrrhanol C and derivatives, a polypodane-type triterpenes. Myrrhanol C was found to trigger apoptosis in chemo resistant, androgen-independent human prostate cancer cells in vitro and in vivo. The industrially-available myrrhanol C may serve as a lead compound for targeting prostate cancers.

Main Advantages: The synthesis procedure has a convergent, and highly stereocontrolled route. Easily scalable procedure.

Applications: Production of pharmaceutical compounds for Urology, Nephrology, and Oncology.

Development Status: Produced in laboratory in miligrams (mg) scale.

Gel of melatonin against mucosa damage

Priority: October 2011.

Features: New pharmaceutical formulation of melatonin (N-acetyl-5-metoxy-tryptamine) in gel, for human and animal topic application. The gel provides excellent protection against oral and gastrointestinal mucosa damage from any source, including radiotherapy. Specifically, this melatonin gel formulation constitutes the first line of treatment to prevent the development of oral mucositis. Experimental studies showed a protection against the acute mucositis induced by radiotherapy, and a decrease of fibrosis with topical gel melatonin application.

Main Advantages: There is not current treatment for radiotherapy-induced mucositis. Melatonin it is easily available at low cost from vegetal origin, and displays long stability. Melatonin has low toxicity, even at high dose.

Applications: Human and veterinarian use. Applicable to all pathologies coursing with mucositis and/or oxidative stress and inflammation.

Development Status: In vivo (rats) and clinical assays. Now it is starting its GMP production.

Antiparasitic scorpiand-type compounds

Priority: December 2011

Features: The invention claims new scorpiand-type azamacrocycle compounds and their use for the treatment of parasitic diseases, specifically for Chagas' disease and leishmaniasis. The synthesised compounds are structurally different from drugs in use, are ten times less toxic and show activity against both, the acute and chronic phases of the infection caused by *Trypanosoma cruzi* and *Leishmania spp.*

Main Advantages: Decrease in price and in the development of side effects due to lower IC50 value of the compounds than drugs in use. Lower toxicity of the compounds than existing drugs for the treatment of Chagas' disease and leishmaniasis. Antiparasitic activity in the chronic phase of the disease.

Applications: Treatment of human or animal parasitic diseases.

Development Status: Assays developed in vitro and as well in vivo (mice).

Glutamyl aminopeptidase as a marker of renal damage

Priority: November 2010. PCT Applied.

Features: Fluorimetric determination of glutamylaminopeptidase activity in urine. This enzyme is localized in renal tubular epithelium and its presence in urine indicates renal damage. The main purpose is the monitoring and diagnosis of pathologies that are accompanied with renal damage. We have demonstrated its efficiency as a marker in several animal models of renal damage, and also in patients with renal failure, cardiorrenal syndrome and transplanted patients.

Main Advantages: Its urinary excretion precedes to other markers, and it can predict the extent of renal dysfunction. Other advantages are the sensitivity of the method, the lack of interferences, the low cost and the possibility to perform serial determinations.

Applications : Cardiovascular, Clinic, Drug Safety and Toxicology, Endocrinology

Development Status: Tested in rat and human samples.

Taiwaniaquinoids and related compounds for cancer treatment

Priority: March 2012

Features: This patent protects the taiwaniaquinoids (terpenoids) and related compounds antitumor properties for use in treating solid tumors such as neuroblastoma, breast, lung, colorectal, liver and pancreas cancer, and against acute and chronic myeloproliferative syndromes, both in humans and animals. These compounds have shown a great capacity to inhibit the growth of human tumor cells.

Main Advantages: The families of compounds comprise a wide group of molecules, some of them naturally occurring. High antitumor activity and therapeutic index values. Rapid obtention at very low cost.

Applications: Cancer, Chemotherapy, Pharmacogenetics

Development Status: Synthetic routes optimized. In vitro antitumoral trials have been completed.

Composition for skin and mucosal bacterial infections

Priority: July 2012

Features: New pharmaceutical formulation based on an anti-bacterial protein called AS-48 in combination with an synergic enhancer of its activity, which its use in controlling and eliminate *P. acnes* and *Staphylococcus* species involves in skin infections, including acne.

Main Advantages: Activity and stability is superior to most of the bacteriocines described for the mentioned pathogens. Absence of toxicity and irritation in breast and skin cell lines.

Applications: Drug Safety and Toxicology , Endocrinology , Inflammation

Development Status: Tested in vitro. Starting clinical trials among healthy people and people with bacterial infections.

ugr | Universidad de Granada

Licensing Opportunities
In Pharma

This brochure contains a sample of the newest patented inventions in Pharmaceutics developed in the University of Granada.

All these technologies are available for licensing or developmental collaborations.

If you want more information about them, please visit our R+D Offer website, http://ofertaimasd.ugr.es, or contact us at otri@ugr.es.

otri | OFICINA DE TRANSFERENCIA DE RESULTADOS DE INVESTIGACIÓN

http://otri.ugr.es
otri@ugr.es
(+34) 958 244 337

Injectable preparation of melatonin

Priority: May 2011. PCT Applied

Features: Pharmaceutical melatonin preparation for human and animal use, based on an aquous, stable solution of melatonin that can be autoclaved. Can be used for intramuscular, intravenous, subcutaneous, intraperitoneal, and any other injectable way of administration. Use related to the regulation of the circadian rhythm, inflammatory response, oxidative stress, and the treatment of sepsis.

Main Advantages: Can be dissolved in the physiological saline solutions. Increases both its half-life and bioavailability, improving the pharmacological effects of the hormone. Physiologically tolerable . Low risk of allergies, side effects, adverse events or other similar reactions. This composition not contain pyrogens.

Applications: Treatment of multiple organ dysfunction syndrome (MODS), of sepsis in neonates, myocardial infarctions, of Mitochondrial damage, pulmonary edema, renal or hepatic failure, and oxidative stress caused by surgery.

Development Status: Starting Clinical Assays and GMP production.

New effective drug against Leishmania

Priority: September 2011. PCT Applied

Features: New drugs effective for the treatment of the antileishmaniasis in animals (including dogs) and humans were obtained. The *in vivo* evaluation has shown a significant reduction of parasites in target organs. The in vitro assay showed their effectiveness against *Leishmania infantum* in infected macrophages (low micro molar scale). The synthesis has been accomplished using a short and easy to scale up scheme.

Main Advantages: The *in vivo* assay has shown a significant reduction of parasites in target organs of the animal model. These new drugs have been synthesized using a short and easy to scale up scheme. It is a mechanistically new approach for the treatment of the Leishmaniasis. The new drugs are potent against the parasite but not against human cells.

Applications: Treatment of leishmaniasis in animals and humans.

Development Status: More *in vivo* assays using infected mice are underway. Several doses of a selected drug are being evaluated.

Cationic Soft Nanocarriers

Priority: March 2010. PCT Applied

Features: Nanometric biocompatible cationic polymeric materials dispersed in water or in an aqueous media (e.g., biological fluid). Sensitive to changes in temperature and/or pH of the medium. When the temperature or pH of the medium in which they are dispersed changes, their volume changes passing from a swollen state to a collapsed one, this transition is reversible. They work as "sponges" of nanometric size: swelling and shrinking.

Main Advantages: They are very interesting to be used as carriers of drugs/active agents. They just have to be loaded and directed to the target. Once there, by changing the temperature or pH the load will be released. They can be stored in a dry state (lyophilized) with or without drug-load and they can be re-dispersed in water or active biological dispersion just when needed.

Applications: Pharmaceutical industry. Carriers for drugs o active agents.

Development Status: Tested in vitro.

Isolation of geranyl-geraniol from a natural resource

Priority: July 2012

Features: A selective extraction method for isolating active constituents with an appropriate organic solvent. These extracts were hydrolyzed in basic medium yielding a pure stereoisomeric product. Geranyl-geraniol is a natural product with applications in the pharmaceutical industry as antitumoral agent and as starting material for Vitamin E synthesis.

Main Advantages: The present method remarkably simplifies the steps number needs to preparation of geranyl-geraniol increasing the efficiency of other described procedures Nowadays a great majority of the processes for industrial preparation of geranyl-geraniol are multi-step synthesis being the separation of geometric isomers the principal troublesome.

Applications: Production of antitumoral agents against leukaemia. Starting material for the Vitamin E synthesis.

Development Status: Production in Laboratory

Anticarcinogenic compounds with kinase activity inhibition

Priority: March 2010. PCT Applied.

Features: This invention claims the two enantiomers of a benzo-fused seven-membered ring linked to purines, and used as anti-tumour agents, preferably against breast, colorectal, melanoma, lung and pancreas cancers and myeloproliferative syndromes. Compounds produce an inhibition of the kinase activity present in the membrane (EGFR) and other localized in the nucleus (VEGF). They possess a high anti-tumour activity and induce a high level of apoptosis in tumour cells. Neither signs of short- nor long-term acute and chronic toxicity were assessed on mice.

Main Advantages: Specificity over tumour cells. Null toxicity shown over non-tumour cells. Powerful tyrosine kinase inhibition. Both enantiomers induce p53 independent- apoptosis and dependent of the protein kinase PKR. Both enantiomers are capable of inducing non-functional apoptosis on cells with non-functional p53, as well as on tumours with a mutated p53 (> 50% of the malignant tumours).

Applications: Oncology.

Development Status: *In vitro* and *in vivo* toxicity assays have been carried out

Test for the determination of PKR as a biomarker of hemotherapy response

Priority: February 2011. PCT Applied

Features: PKR is a molecular target of 5-FU inducing cancer cell death by apoptosis in a p53 independent manner. PKR-deficient cells were more resistant to 5-FU that cells exppressing active PKR. Therefore, PKR is a potential biomarker of 5-FU-based chemotherapies.

Main Advantages: Since alterations in the mediators of 5-FU-induced apoptosis may account for chemo resistance, the identification of PKR which is involved in the 5-FU-induced apoptosis in a p53-independent manner. The analysis of additional prognostic and preventive molecular markers such as PKR has a significant clinical interest in patients where p53 is mutated.

Applications: Oncology, Personalized Medicine of cancer

Development Status: Validate in vitro (tumor cells) and pre-clinical assays

Deuterium labeled Fenucil and Uracil

Priority: December 2010. PCT Applied

Features: Deuterium labeled fenucil (DLF) and other uracil derivatives (DLUD) are novel thyrostatic drugs. They might be used to analyze samples of livestock dishonestly put on weight with Fenucil by HPLC-MS. They can also be used for metabolic studies on Fenucil and Uracil derivatives. In these patents the chemical synthesis and HPLC-MS analysis of DLF and DLUD are presented.

Main advantages: DLF and DLUDF have not been reported previously. Moreover, DLUD are easy to prepare at low cost. It is presumably that DLUD could have more prolonged pharmacological properties than conventional Uracil derived thyrostatic drugs.

Applications: Endocrinology

Development Status: Both the chemical synthesis and the HPLC-MS analysis of DLF and DLUD have been completed.

Cyclophanes with antileishmanial and antiprotozoal activities

Priority: August 2012

Features: This invention shows cyclophanes with leishmanicidal and protozoacidal properties and to the use thereof as drugs for human and animal vertebrates, and a method for the preparation of the target compounds and several intermediates. Compounds produce a depolarization of mitochondria and subsequent drop of the ATP levels, which leads to the parasite death by means of an energetic collapse.

Main Advantages: These cyclophane derivatives that can be used for the treatment of visceral and cutaneous leishmaniasis have the advantage of being more active and less toxic over promastigote and intracellular amastigote forms than the reference compounds amphotericin B and miltefosine.

Applications: Treatment of human or animal parasitic diseases

Development Status: *In vitro* toxicity assays have been carried out.

Polymeric nanoparticles comprising Poli(ξ-Caprolactone) y Doxorubicin

Priority: March 2011. PCT Applied

Features: Polymeric nanoparticles, with an average size less than 200 nm, which comprises one or more biodegradable polymers, active ingredients and a surfactant, wherein at least one biodegradable polymer is poly (ξ--caprolactone) and where the active substance is doxorubicin, for the preparation of medicaments for the treatment of cancer, preferably breast cancer.

Main Advantages: Nanoparticles provide a high anticancer agent vehiculization and reach a very high extravasation into the tumor mass and, in turn, a more controlled release thereof. Significant increase of the antitumor activity when nanoparticles ares used as vehicles for delivery of anticancer drugs

Applications: Drug delivery. Oncology

Development Status: Tested in vitro