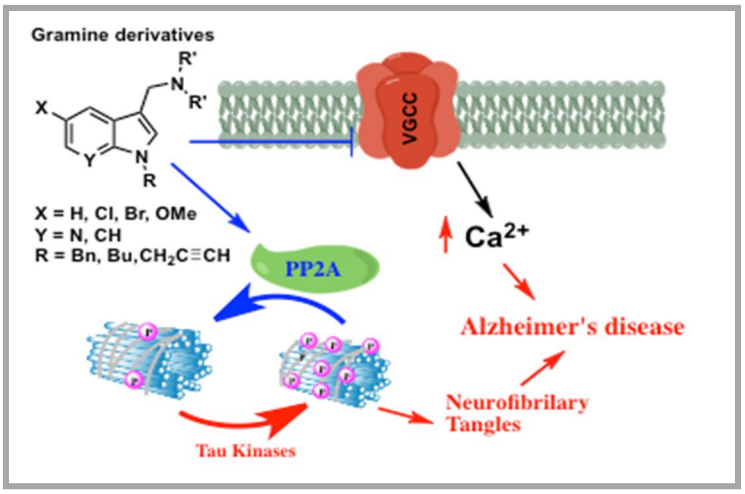
Technology Offer

New Gramine derivatives with up-regulating activity of phosphatase enzymes and their application in the treatment of human disesase

BRIEF SUMMARY: Several years ago, *La Princesa Institute for Health Research* (research group led by Dr. Cristóbal de los Ríos), in collaboration with Universidad Autonoma de Madrid and the Teofilo Hernando Foundation, paid attention to the interesting properties of a natural product called gramine. These properties were related to an activating profile of phosphatases. We disclose the preparation of newly synthesized gramine derivatives with extended phosphatase-activating profile, as well as blocking effect of neuronal voltage-gated Ca^{2+} channels (VGCC). Thus, these new compounds, which present potential good pharmacokinetic profile, exert neuroprotection in several *in vitro* models of neurodegeneration.

MAIN FEATURES:



There is a current interest in developing new drugs able to interact with two or more biological targets implicated in CNS diseases, viral infections, or cancer, among others, under the so-called multitarget-based drug design (MTDD) approach. Examples of this strategy are found in. The compounds claimed in this memo focus on improving the phosphatase activity, mainly of the Ser/Thr phosphatase PP2A, which is an enzyme implicated in a plethora of chief cellular process, where its depression or inhibition have been evidenced in a huge amount of tumours, neurodegenerative diseases, and viral infections. Sadly, the PP2A-activating drugs (PADs) have raised marginal interest

compared with the huge investment paid to the counterpart kinase enzymes inhibitors, although the therapeutic response offered would be similar. This offer aims to demonstrate the eligibility of PADs as potential drugs with therapeutic interest, in the context of a MTDD strategy. These compounds blocked VGCC and protected PP2A activity, what derived in a neuroprotective signal against toxic stimuli related to neuronal damage.

THERAPEUTIC AREA: Although most of the experiments were designed to claim their use for neurodegenerative diseases, the lack of medicines featuring similar biological activities, and the implication of PP2A impairment in a huge amount of human diseases, highlighting cancer or neuropathic pain, prompt us to claim their use not only in neurodegeneration, but also in several types of cancer, pain, and in all those diseases that entail a depression of the PP2A-leaded phosphatase activity.

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IPR STATUS: Patent application filed in Spain. PRIORITY DATE: 10/10/2017

PARTNERSHIP CONSIDERED: Licensees or research cooperation.

References

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