Speaker information

General Information

Name	Filippo Cottiglia	
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Contact Number	+390706758979	
Affiliation	Department of Life and Environmental Sciences, University of Cagliari	
Education Background	He graduated at the University of Cagliari (1993) in Medicinal Chemistry and Technology with 110/110 points, summa cum laude. In 1997 he reached a PhD degree in Medicinal Chemistry, University of Cagliari, under the supervision of Prof. Leonardo Bonsignore. In 1998-1999 awarded postdoctoral exchange of study grant at the University of Cagliari. In 2000 he was awarded the title of Specialist in Industrial Pharmacy, University of Pavia, Italy. In 2000-2001 he was postdoctoral fellow in the group of Prof. Dr. Otto Sticher, Pharmacognosy and Phytochemistry, Institute of Pharmaceutical Sciences, Swiss Federal Institute of Technology (ETH) Zurich, Switzerland. He was appointed Assistant Professor of medicinal chemistry in 2002. Since 2019 Associate Professor in Medicinal Chemistry at the Department of Life and Environmental Sciences, University of Cagliari.	
Research Interest	His research focuses on isolation, structure elucidation and biological screenings of natural products from medicinal plants. In particular, he is interested in metabolites which show antitumor, anti-inflammatory and antiviral activity, as well as interaction with cannabinoid and GABA receptors. In particular, he has a long-standing experience in chromatographic techniques and a deep knowledge in NMR experiments devoted to the structure elucidation of natural compounds including one dimensional (^{1}H and ^{13}C NMR, APT) and two dimensional NMR (COSY, HSQC, HSQC-TOCSY, HMBC, NOESY, ROESY). He is also interested in HPLC enantioseparation of racemic mixtures and synthesis and semi-synthesis of natural products analogues.	

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Website	https://web.unica.it/unica/page/it/filippo_cottiglia

Recent Publications

1. Huang SW, Hsu MJ, Chen HC, Meleddu R, Distinto S, Maccioni E, Cottiglia F. Suppression of lipopolysaccharide-induced COX-2 expression via p38MAPK, JNK, and C/EBPb phosphorylation inhibition by furomagydarin A, a benzofuran glycoside from Magydaris pastinacea. Journal of Enzyme Inhibition and Medicinal Chemistry 2024, 39, 287420.
2. Corona A, Meleddu R, Delelis O, Subra F, Cottiglia F, Esposito F, Distinto S, Maccioni E, Tramontano E. 5-Nitro-3-(2-(4-phenylthiazol-2-yl)hydrazineylidene)indolin-2-one derivatives inhibit HIV-1 replication by a multitarget mechanism of action. Frontiers in Cellular and Infection Microbiology 2023, 13,1193280.
3. Maccioni R, Serra M, Marongiu J, Cottiglia F, Maccioni E, Bassareo V, Morelli M, Kasture SB, Acquas E. Effects of docosanyl ferulate, a constituent of Withania somnifera, on ethanol- and morphine-elicited conditioned place preference and ERK phosphorylation in the accumbens shell of CD1 mice. Psychopharmacology 2022, 239, 795–806.
4. Firoznezhad M, Castangia I, Tuberoso CI, Cottiglia F, Marongiu F, Porceddu M, Usach I, Escribano-Ferrer E, Manca ML, Manconi M. Formulation and In Vitro Efficacy Assessment of Teucrium marum Extract Loading Hyalurosomes Enriched with Tween 80 and Glycerol. Nanomaterials 2022, 12, 1096.
5. Fois B, Corona A, Tramontano E, Distinto S, Maccioni E, Meleddu R, Caboni P, Floris C, Cottiglia F. Flavonoids Acid-Hydrolysis derivatives of Neo-Clerodane diterpenes from Teucrium flavum subsp. Glaucum as inhibitors of the HIV-1 reverse transcriptase–associated RNase H function. Journal of Enzyme Inhibition and Medicinal Chemistry 2021, 36, 749-757.
6. Meleddu R, Deplano S, Maccioni E, Ortuso F, Cottiglia F, Secci D, Onali A, Sanna E, Angeli A, Alcaro S, Supuran CT, Distinto S. Selective inhibition of carbonic anhydrase IX and XII by coumarin and psoralen derivatives. Journal of Enzyme Inhibition and Medicinal Chemistry 2021, 36, 685-692.
7. Maccioni R, Cottiglia F, Maccioni E, Talani G, Sanna E, Bassareo V, Kasture S, Acquas E. The biologically active compound of Withania somnifera (L.) Dunal, docosanyl ferulate, is endowed with potent anxiolytic properties but devoid of typical benzodiazepine-like side effects. Journal Psychopharmacol 2021, 35: 1277-1284.
8. R. Meleddu, S. Distinto, F. Cottiglia, R. Angius, P. Caboni, A. Angeli, C. Melis, S. Deplano, S. Alcaro, F. Ortuso, C.T. Supuran, E. Maccioni. New Dihydrothiazole Benzensulfonamides: Looking for Selectivity toward Carbonic Anhydrase Isoforms I, II, IX, and XII. ACS Medicinal Chemistry Letters 2020, 11, 852–856.
9. B. Fois, S. Distinto, R. Meleddu, S. Deplano, E. Maccioni, C. Floris, A. Rosa, M. Nieddu, P. Caboni, C Sissi, A. Angeli, C. T. Supuran, F. Cottiglia, "Coumarins from Magydaris pastinacea as inhibitors of the tumor-associated carbonic anhydrases IX and XII: isolation, biological studies and in silico evaluation", Journal of Enzyme Inhibition and Medicinal Chemistry 2020, 35, 539-548.
10. V.P. Sonar, B. Fois, S. Distinto, E. Maccioni, R. Meleddu, F. Cottiglia, E. Acquas, S. Kasture, C. Floris, D. Colombo, C. Sissi, E. Sanna, G. Talani. Ferulic acid esters and withanolides: in search of Withania somnifera GABAA receptor modulators. Journal of Natural Products 2019, 82, 1250-1257.

Speaker information

Speech Topic and Abstract

Title:

Natural product-inspired GABA receptor complex modulators

Abstract:

γ-Aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the vertebrate central nervous system and interacts physiologically with two types of receptors, designated $GABA_A$ and $GABA_B$. $GABA_A$ receptors are ligand-activated Cl- channels, whereas $GABA_B$ receptors are coupled to G proteins. $GABA_A$ receptor full agonists exhibit anxiolytic, hypnotic, and anticonvulsant activities. On the contrary, the metabotropic $GABA_B$ receptors mediate slow inhibitory transmission and regulate the presynaptic release of GABA. $GABA_B$ agonist and allosteric modulators show antispastic activity and are effective in treatment of alcohol abuse and drug addiction.

The Ayurvedic plant Withania somnifera is used to treat various neurological disorders, insomnia, anxiety, stress, and behaviour-related problems. Both clinical and animal studies have supported the traditional use of W. somnifera as an antistress and anxiolytic remedy.[1,2] Recently, we identified from the methanol extract of the roots of W. somnifera a secondary metabolite, docosanyl ferulate (DF), able to enhance the $GABA_A$ receptor inhibitory postsynaptic currents.[3] Further studies on mouse behavioural models demonstrated that DF exerts anxiolytic effects modulating the $GABA_A$ receptor complex activity by interacting with the benzodiazepine binding site.[4] Moreover, at the full anxiolytic dose of 2 mg/kg, DF lacks typical benzodiazepine-like side effects on motor and cognitive performances and on place conditioning.[4]

In the light of the interesting results showed by the natural product DF, we synthesized a series of heterocyclic DF analogues. The new compounds were able to modulate the GABA receptor complex, even though with a different mechanism respect to that of DF.

REFERENCES

1. Pratte MA, Nanavati KB, Young V, Morley CP (2014). An alternative treatment for anxiety: A systematic review of human trial results reported for the ayurvedic herb Ashwagandha (*Withania somnifera*). J Altern Complement Med 20: 901–908.
2. Kaur T, Singh H, Mishra R, Manchanda S, Kaur G (2017). *Withania somnifera* as a potential anxiolytic and immunomodulatory agent in acute sleep deprived female Wistar rats. Mol Cell Biochem 427: 91–101.
3. Sonar VP, Fois B, Distinto S, Maccioni E, Meleddu R, Cottiglia F, Elio Acquas E, Kasture S, Floris, Colombo D, Sissi C, Sanna E, Talani G (2019). Ferulic acid esters and withanolides: In search of *Withania somnifera* $GABA_A$ receptor modulators. J Nat Prod 82: 1250–1257.

4. Maccioni R, Cottiglia F, Maccioni E, Talani G, Sanna E, Bassareo V, Kasture S, Acquas E (2021). The biologically active compound of *Withania somnifera* (L.) Dunal, docosanyl ferulate, is endowed with potent anxiolytic properties but devoid of typical benzodiazepine-like side effects. Journal Psychopharmacol 35: 1277-1284.