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Biomolecules of tea

Valérie Rolland, Fatiha Sebih, Janique Guiramand, Catherine Cohen-Solal,
Marie-celeste de Jesus Ferreira, Marc Rolland, Michel Vignes

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BIOMOLECULES of TEA



IBMM
Institut des
Biomolécules
Max Mousseron

Fatiha Sebih^{a, b}, Janique Guiramand^a, Catherine Cohen-Solal^a, Marie-Céleste de Jésus Ferreira^a, Marc Rolland^c,
Michel Vignes^a and Valerie Rolland^a

^a « Oxidative stress and neuroprotection » Team^a, Département DAPP, Institut des Biomolécules Max Mousseron, CNRS UMR 5247, UM2.

^b Laboratoire de synthèse organique appliquée, Département de Chimie, Université d'Oran es Sénia, El M'naouer, 31000 Oran.

^c Institut Européen des Membranes UMR5635, UM2.

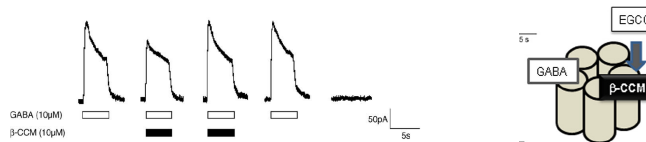
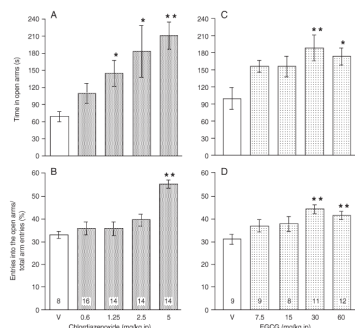
Contacts: valerie.rolland@univ-montp2.fr, michel.vignes@univ-montp2.fr

Introduction:

It is now accepted that green tea consumption is beneficial to human health. Most of these health benefits are associated with **green tea antioxidant activity**. Indeed, potent antioxidants belonging to the catechin family, including **epi-gallocatechin-gallate (EGCG)** are encountered in green tea. Nevertheless, other molecules, such as theanine, a unique amino-acid found in green tea, may also contribute to its beneficial effects.

With regards to the central nervous system (CNS), theanine have proved to be neuroprotective in various models of brain injury, such as ischemia and neurodegenerative diseases. This is due to their ability to cross the blood-brain barrier (BBB). In addition, both molecules seem to exert rapid and long-lasting protective effects. While their long-lasting effects involve genomic actions, rapid effects appear to be restricted to action on neuronal membranes such as the modulation of neurotransmitter receptors.

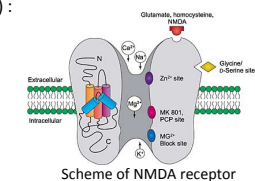
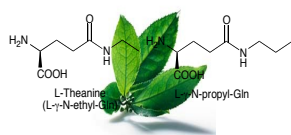
We illustrate here rapid CNS actions of EGCG and theanine with the demonstration of the anxiolytic activity of EGCG, via the modulation of GABA_A receptors and the co-agonist activity of L-theanine towards glutamate N-methyl-D-Aspartate (NMDA) receptors. In this line, derivatives synthesized from the theanine backbone are a new family of NMDA receptor ligands.^{1,2}



EGCG was evaluated for anxiolytic effect by performing the elevated plus maze (EPM) test (left panel). EGCG, just like benzodiazepine drug (chlordiazepoxide), increases the time spent in the open arms of the EPM. This suggests an anxiolytic action of EGCG.

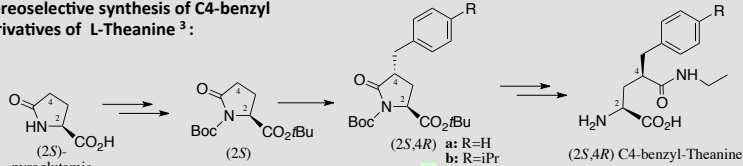
Electrophysiological measurements of GABA_A receptors-mediated currents show that EGCG interacts with the binding site of negative modulators of these receptors.

Theanine (BS68) and N-Propyl Glutamine (BS77) :

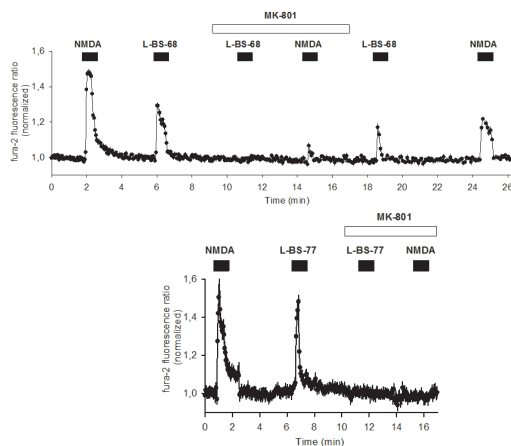
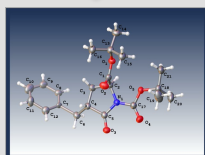


Theanine (BS68) and its N-Propyl derivatives (BS77) (L&D) were tested for their ability to interact with glutamate receptors. For this they were applied on Fura-2-loaded cultured hippocampal neurons and Fura-2 fluorescence was further measured. These compounds elicit intracellular calcium increases which are sensitive to NMDA receptors antagonist MK801. This suggest that theanine derivatives represent a family of new NMDA receptor ligands.

Stereoselective synthesis of C4-benzyl derivatives of L-Theanine³:



Ortep view of (2S,4R)-C4-benzyl-Theanine crystal



Conclusion:

Green tea constituents, ie EGCG and Theanine, may modulate neuronal activity by acting on GABA and glutamate-mediated synaptic transmission likely via an interaction with the receptors of these neurotransmitters.

The structure of these biomolecules could thus be interesting to develop new leads with potential CNS therapeutic activity, as we are currently doing with theanine.

Acknowledgment:

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- « Diastereospecific synthesis of new 4-substituted L-Theanine derivatives » Fatiha Sebih, Salima Bellahouel, Marc Rolland^a, Aicha Derdour, Jean Martinez, Valérie Rolland. *Tetrahedron: Asym.* 2014, 25, 690-696.