

## Pharmacological basis of the anxiolytic and antidepressant properties of Silexan

Walter E. Müller<sup>1</sup>

<sup>1</sup> Department of Pharmacology, Biocenter, Goethe-University Frankfurt, Germany

Silexan®, a proprietary essential oil manufactured by steam distillation from *Lavandula angustifolia* flowers showed pronounced anxiolytic effects in patients with subthreshold anxiety disorders and was also efficacious in patients with Generalized Anxiety disorder (GAD). Moreover, evidences for antidepressant-like properties of Silexan® have been observed in anxious patients suffering from comorbid depressive symptoms and in patients with mixed anxiety-depression disorder (ICD-10 F41.2) 2020). In accordance with the clinical data Silexan® is active in several behavioural models in rodents at rather low concentrations indicating potent anxiolytic and antidepressive properties. As possible mechanism of action a moderate inhibition of voltage dependent calcium channels (VDCC) has been found showing some similarities to the anxiolytic drug pregabalin. However, while pregabalin mainly inhibits P/Q-type channels by binding to a modulatory subunit, Silexan® moderately inhibits mainly T-type and N-type channels and to some extent P/Q-type channels. Unlike pregabalin Silexan® is free of hypnotic or sedative side effects and does not present of any abuse potential. With respect to its specific antidepressant like properties Silexan® improves several aspects of neuroplasticity which seems to be the common final pathway of all antidepressant drugs. As a potential mechanism of its effects on neuroplasticity an activation of the transcription factor CREB via activation of intracellular signaling kinases like PKA and MAPK has been found. Since the concentrations of Silexan® needed to inhibit VDCC function and to improve neuroplasticity are quite similar, the effects of Silexan® on PKA or MAPK could constitute a common intracellular signaling cascade leading to VDCC modulation as well as CREB activation and improved neuroplasticity.

- [1] Schuwald, A.M., Nöldner, M., Wilmes, T., Klugbauer, N., Leuner, K., Müller, W.E., 2013. Lavender oil -Potent Anxiolytic Properties via Modulating Voltage Dependent CalciumChannels. PLoS One 8, e59998.
- [2] Müller W.E., Schuwald A., Nöldner N., Kasper S., F.K., 2015. Pharmacological basis of the therapeutical use of Silexan® (Lasea). *Psychopharmakotherapie* 22, 3–14
- [3] Kasper, S., Müller, W.E., Volz, H.P., Möller, H.J., Koch, E., Dienel, A. 2018. Silexan® in anxiety disorders: Clinical data and pharmacological background. *World J. Biol. Psychiatry* 19: 412-420
- [4] Friedland, K., Silani, G., Schuwald, A., Stockburger, C., Nöldner, M., Koch, E., Müller, W.E. 2020. Neurotrophic properties of Silexan®, an essential oil from the flowers of lavender - preclinical evidence for antidepressant-like properties. *Pharmacopsychiatry*, in press
- [5] Müller, W.E., Sillani, G., Schuwald, A., Froiedland, K. 2020. Pharmacologocal basis of the anxiolytic and antidepressant properties of Silexan, an essential oil from the flowers of lavender, submitted.