

Natural products used in Ayurvedic treatments alleviate symptoms of depression in fruit flies

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The level of motivation of the fruit fly Drosophila can be deduced on the basis of whether it attempts to climb over gaps it encounters when walking. In a depression-like state, the fruit fly is less likely to do so. Credit: Helen Hovoet, Hans-Hermann Huber



Chronic exposure to stress can lead to the development of depressionlike disorders that manifest as a lack of motivation—even in the fruit fly Drosophila melanogaster. As a result, the insects show less courtship behavior, are less interested in stopping to ingest sweet nutrients, and are less willing to climb a gap in the experimental setup.

Traditional <u>medicinal plants</u>, however, can—to some extent—alleviate some of the associated symptoms, as observed by researchers at Johannes Gutenberg University Mainz (JGU) in Germany in collaboration with the BENFRA Botanical Dietary Supplements Research Center in Portland, Oregon.

The researchers have shown that two plants used in Ayurvedic medicine can improve resilience to chronic stress when used prophylactically in the flies. Despite their stressed state, they then no longer displayed behavior consistent with depression. <u>Papers</u> on their <u>studies</u> of the two plant materials have been published in *Nutrients*.

Plants containing biologically-active ingredients can help the organism deal with stress

The JGU research group led by Professor Roland Strauss has been using the Drosophila melanogaster model to analyze the underlying mechanisms involved in resilience to stress and the <u>effects of stress</u> on the nervous system.

"Chronic stress can induce depression-like states also in the fruit fly, and these become apparent in changes to their behavior," explained Strauss. In this most recent research context, his group cooperated with the BENFRA Botanical Dietary Supplements Research Center in the United



States of America. The center investigates botanicals that enhance neurological and functional resilience in aging.

The Mainz-based researchers focus on testing extracts of botanicals and <u>natural substances</u> that are known to be used in traditional Asian medicine and are also marketed as dietary supplements. The idea is that certain plants contain above-average amounts of active constituents or substances that themselves demonstrate particularly high levels of biological activity. These so-called adaptogens can help our bodies adapt to increased physical and emotional stress.

"An advantage over conventional drugs could be that medicinal plants contain blends of various active botanical substances that act on different sites of the stress axis," said Helen Holvoet, a doctoral candidate in the team of Professor Strauss and lead author of the two papers.

"Because they have a synergistic effect on counteracting stress, they may cause fewer undesirable effects than if the substances themselves were administered alone in pure form." Another potential advantage is that dietary supplements can be used as complementary medication in association with pharmacotherapies.





The uptake of sugar and adaptogens can alleviate and even prevent depressionlike states in the fruit fly Drosophila. Credit: Tim Hermanns

In the joint project, Strauss' team tested their approach for the treatment of stress using two Ayurvedic medicinal plants, namely Withania somnifera (known as ashwagandha or the sleep berry) and Centella asiatica (the Indian pennywort). The research partners were able to demonstrate that, when administered prophylactically, both plants



enhanced the resilience to <u>chronic stress</u> so that the flies exposed to stress did not get into a depression-like state in the first place.

Chlorogenic acid identified as substance relevant to the treatment of stress

"In the case of Withania somnifera, we found that the way of preparing the root makes a difference—as aqueous extracts provided better prophylactic effects than extracts in alcohol," explained Dr. Burkhard Poeck, who was also involved in the experiments. This surprising result does indicate how important it is to pay attention to the production methods used for dietary supplements.

The team in Mainz and their cooperation partners in Portland obtained an even more impressive result when experimenting with Centella asiatica. They were actually able to identify a specific component, <u>chlorogenic acid</u>, acting as a prophylactic, anti-stress substance. Chlorogenic acid is present in many botanicals, in particularly high levels in coffee beans, for example. It is also found in traditional medicinal herbs such as valerian (Valeriana officinalis) and St. John's wort (Hypericum perforatum), the stress-relieving potential of which have long been known.

The analysis of such medicinal substances not only provides general information on their effects on neuronal <u>stress</u>, but it can also offer starting points for fundamental resilience research.

"In this case, we were able to pinpoint a relevant target protein for chlorogenic acid in Drosophila, the protein phosphatase calcineurin," said Professor Roland Strauss, explaining additional research results. In humans, calcineurin is present in many body organs and there are exceptionally high concentrations in the nervous system. There it



interacts with numerous other proteins and mediates many signaling pathways.

More information: Helen Holvoet et al, Chlorogenic Acids, Acting via Calcineurin, Are the Main Compounds in Centella asiatica Extracts That Mediate Resilience to Chronic Stress in Drosophila melanogaster, *Nutrients* (2023). DOI: 10.3390/nu15184016

Helen Holvoet et al, Withania somnifera Extracts Promote Resilience against Age-Related and Stress-Induced Behavioral Phenotypes in Drosophila melanogaster; a Possible Role of Other Compounds besides Withanolides, *Nutrients* (2022). <u>DOI: 10.3390/nu14193923</u>

Provided by Johannes Gutenberg University Mainz

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