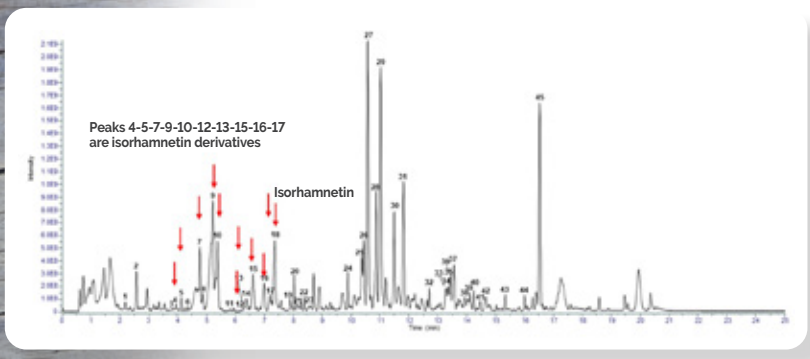
OLIVELax®

Hippophae rhamnoides L.
High quality dry extract standardized in isorhamnetin

The extract shows a **very rich phytocomplex**; 75 compounds have been detected by chromatographic technique (UHPLC-HRMS/MS) including:

- **flavonoids**,
- phenolic acids,
- proanthocyanidins,
- carotenoids,
- triterpenoids.

Sea buckthorn fruit also contains **mannitol**.



Constipation is a clinical condition characterized by several symptoms, including **hard or lumpy stools**, **abdominal discomfort**, **infrequent or difficult bowel movements**, and a **sensation of incomplete evacuation**; it affects approximately **9-20% of the global population**, **women** and **older adults** most frequently, with a significant impact on their **quality of life**.

Sea buckthorn fruits have been **traditionally used as a purgative** since the 16th century **(1)**. Laxative and prokinetic effects of sea buckthorn have been demonstrated *in vivo* through partial activation of **muscarinic receptors**; on the other hand, the presence of **inhibitory phytochemicals** could **avoid** the **typical adverse effects** (abdominal cramps) of **parasympathomimetic drugs (2)**.

REFERENCES: (1) Campanini E., Dizionario di fitoterapia e piante medicinali, II Ed. Tecniche Nuove, 2006
(2) Hanif M.; Mehmood M.H.; Ishrat G.; Abdullah A.; Sohail S.; Ahmed M.; Gilani AH. Evaluation of prokinetic and laxative effects of Hippophae rhamnoides in rodents. Pak J Pharm Sci. 2019 Sep;32(5(Special)):2527-2533. PMID: 31894044.

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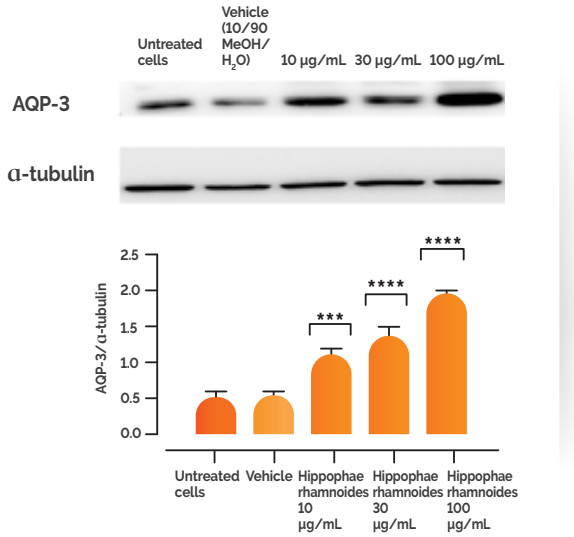
PRECLINICAL STUDIES

OLIVELLAX® up-regulates the proteic expression of AQP-3

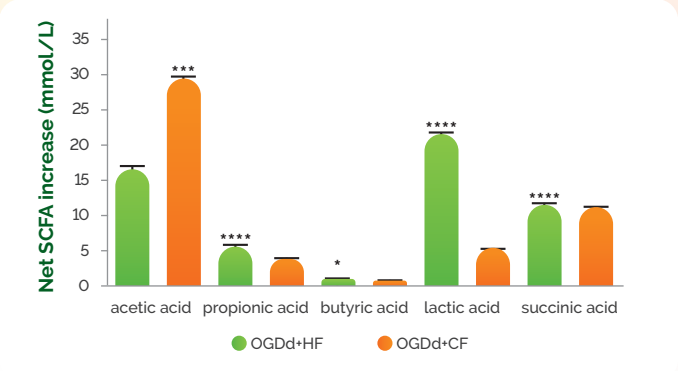
Aquaporin-3 (AQP-3) is a **water channel protein** predominantly expressed **in the colon**; modulating AQP-3 expression seems to relieve constipation by **enhancing stool hydration**. Olivellax® **significantly up-regulates AQP-3 expression compared to the vehicle control,** improving the passage of water into the gut lumen; this suggests an **osmotic laxative-like** mechanism of action **(1)**.



Effect of Olivellax® on AQP-3 expression. Colon-rectal adenocarcinoma epithelial (HT-29) cells were treated for 24 h with the extract or vehicle (10/90 methanol/water). ***p<0.001, ******p<0.0001

After fecal fermentation, the digested OLIVELLAX® improves SCFAs levels

It is well known that **altered gut microbiota (dysbiosis)** contribute to **constipation**; **SCFAs** (Short Chain Fatty Acids) are **produced** by **gut microbiome fermentation** of **dietary fiber**; a **key energy source** for **colon cells,** they play an important role in **gut functionality**; propionic and butyric acid affect intestinal motility by directly acting on **colonic smooth muscle**, stimulating the release of **serotonin** (5-HT). **SCFAs** are known to be **significantly reduced** in **subjects with constipation**.



SCFAs produced by gut microbiota of healthy and constipated adults after fermentation of the digested Olivellax®. Data are presented as the means ± SD. *p<0.05, ***p<0.001, and ****p<0.0001

Fecal samples from **healthy subjects** (green bars) are richer in **lactic**, **succinic**, **propionic**, **and butyric acids**, while those from the **constipated group** (orange bars) show an increased concentration of **acetic acid**.
This suggests that *H. rhamnoides* fruit extract (Olivellax®) **helps restore SCFAs levels** in constipated subjects whereas in healthy subjects the extract could maintain optimal SCFAs levels **(1)**.

To validate these preliminary preclinical results and provide a more comprehensive understanding of the extract's mechanism of action, a **randomized**, **double-blind**, **placebo-controlled**, **parallel-arm clinical trial** was conducted in **subjects with functional constipation** diagnosed with **Rome IV criteria**; the results show a **significant improvement** in **constipation symptoms**, such as **number of evacuations per week** and **stool consistency**, with **no adverse effects (2)**.

REFERENCES: (1) De Lellis, L.F.; Toledano-Marín, Á.; Navarro-Moreno, M.; Caiazzo, E.; Madonna, G.; Delgado-Osorio, A.; Buccato, D.G.; Izzo, L.; Paolillo, A.; Di Minno, A.; et al. In Vitro Influence of a Chemically Characterized Hippophae rhamnoides L. Fruit Extract on Healthy and Constipated Human Gut Microbiota Functionality and Aquaporin-3 Expression. Foods 2025, 14, 3800. https://doi.org/10.3390/foods14213800. **(2)** Unpublished data (2025).

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