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## Extract Rheum rhaponticum (ERr) 731: A Promising Alternative for Menopausal Symptom Relief

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### SUMMARY

The present paper discusses the clinical application and scientific evidence of the special Extract Rheum rhaponticum (ERr) 731, derived from the roots of the rhapontic rhubarb. Originally used to treat irregular menstrual cycles, ERr 731 is now primarily employed to alleviate menopausal symptoms. The extract has a similar mode of action to estrogens, has been found to be a highly selective ER $\beta$  agonist, and showed to be clinically safe and effective. Studies suggest that ERr 731 can reduce anxiety, depressed mental state, sleeping disorders, and hot flushes more effectively than low-dose hormone therapy. Furthermore, unlike certain synthetic hormones, ERr 731 is not listed as an endocrine disrupting chemical and may serve as a more environmentally friendly alternative. It has advantages in terms of crop yield, resistance against pests and diseases, and reliable production. Overall, ERr 731 may offer significant benefits for patients and manufacturers.

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### INTRODUCTION

Rhapontic rhubarb has a broad range of applicability in traditional medicine and contemporary herbal therapies (Kolodziejczyk-Czepas & Liudvytska, 2021). While rhubarb root (*Rheum officinale*) is an anthraquinone containing drug, which is used in phytotherapy in the treatment of obstipation (European Medicines Agency (EMA), 2020), the special Extract Rheum rhaponticum (ERr) 731, from the roots of the rhapontic rhubarb has been used in gynaecology in Germany as prescription or pharmacy-only drug since the 1950s (Rote Liste, 1957) and since 2010 abroad as New Dietary Ingredient (US Food & Drug Administration, 2023). While the extract has initially been used to treat irregularities of the menstrual cycle in younger women (Göppingen, 2001), it is now primarily applied to treat menopausal symptoms. The 4 mg dosage ERr 731 is provided in enteric-coated form to prevent potential nausea. This

paper reviews the current practice and scientific evidence related to the clinical application of ERr 731.

### MATERIALS AND METHODS

A comprehensive review of the scientific literature related to the clinical use of ERr 731 was performed and is summarized in the present paper.

### RESULTS AND DISCUSSION

Menopausal hormone therapy is associated with health risks for women (Collaborative Group on Hormonal Factors in Breast Cancer, 2019). The dry extract ERr 731 consists mainly of rhaponticin (<90%) and aglycones (5%) of rhaponticin and desoxyrhaponticin. In plants, these natural hydroxystilbene compounds share a common biosynthetic pathway with resveratrol. Clinical observations suggest that the mode of action of ERr 731 is similar to that of hormones (i.e., estrogens).

ERr 731 has been found to be a highly selective estrogen receptor (ER)  $\beta$  agonist (Vollmer et al., 2010) and its clinical efficacy, safety and effectiveness have been proven in humans (Chang et al., 2016; Kolodziejczyk-Czepas & Liudvytska, 2021). A state of the art review related to Rhaponticin, a stilbene compound found in rhapontic rhubarb, also confirmed its anti-inflammatory properties, which may enhance its health-promoting actions or pharmacological potential (Kolodziejczyk-Czepas & Liudvytska, 2021).

ERr 731 has been found to lead to improvements in patient's anxiety, depressed mental state, and sleeping disorders. The studies show that hot flushes and sweating could be reduced more with ERr 731 after 12 weeks as compared to low dose hormone therapy using 0.1 and 0.25 Norethisteron-Acetat (Heger, 2010).

Based on the current body of evidence, Rhapontic rhubarb is already used medicinally in selected health care systems and has recently been added to the so called most reliable S3-guideline of the German Society of Gynecology and Obstetrics (Klose & Langhorst, 2020). The evaluated evidence related to the phytotherapeutic drug was found to be sufficient to show its effectiveness in the treatment of climacteric disorders. Also, contrary to other endocrine disrupting chemicals like estrogen, rhapontic rhubarb has not been put on the so-called watch list related to the enforcement of the Drinking Water Directive of the European Union and may therefore be considered a future-oriented alternative to such constituents. Drug manufacturers may have to contribute significantly to water cleaning from synthetic hormones (McKie, 2012).

Further advantage of *Rheum rhaponticum* is that it is easy to crop, achieves a higher yield with fertilisers and having a high resistance against pests and diseases. An internal morphological taxonomy, identification and authentication exists at the manufacturer. The sustainable supply chain with the patented manufacturing method enables unfailing production, which is continuously monitored through pharmaceutical-technological process steps.

## CONCLUSIONS

Studies on ERr 731 prove its safety and effectiveness. ERr 731 may pose distinct advantages over hormone therapy for both, patients and manufacturers.

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