



Letter to the Editor

**Subject: Contribution of Maistro et al. in Genetics and Molecular Research
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Dear Dr. Duarte,

The authors of this letter have read with interest the article “Genotoxicity and mutagenicity of *Rosmarinus officinalis* (Labiatae) essential oil in mammalian cells *in vivo*”, published in Genetics and Molecular Research 2010; 9(4): 2114-2122. Maistro and co-workers investigated the genotoxic and mutagenic potential of rosemary essential oil in *ex vivo* studies (rodents) using the comet, micronucleus and chromosome aberration assays. However, their article raises various questions about its scientific quality and accuracy.

1. Characterization of the rosemary oil: The authors used dried crushed aerial parts with botanical identification as *R. officinalis*, which had been imported from Turkey. It is unclear, whether skilled authorized persons (e.g., botanist) had ascertained its botanical identity and determined the purity prior to the extraction of the oil, as plant material can be adulterated by other plants and/or contaminated, e.g., by pesticides. Furthermore, a chemical analysis of the distilled rosemary oil is also missing. This information is essential for performing the tests in the present publication in a scientifically correct manner and should have been requested by the reviewers.

2. Harmful side effects: In the Introduction, the authors stated: “However, po-

tential harmful side-effects of rosemary oil have been described". To support this, they cited a paper from Lemonica et al. (1996). In this publication 26 mg of a 30% (w/v) *R. officinalis* aqueous extract (13 mg solids/mL) made from leaves, flowers and stem was given orally to pregnant Wistar rats during either the preimplantation or the organogenic period. The extract did not cause significant changes in the postimplantation loss or in the number of anomalies or malformations of the term fetuses. In contrast to the statement by Maistro et al., Lemonica et al. (1996) did not use the oil component of the plant. The chemical composition of aqueous extracts of the aerial parts of rosemary differs from that of the oil from rosemary leaves or from the aerial parts. Therefore, it is scientifically incorrect to suggest that the biological activity of rosemary oil from the aerial parts can be deduced from experimental results obtained using aqueous extracts. The same holds true for similar statements by the authors in the Discussion section (see page 2120; citations: Gaiani et al. (2006), who used a hydro-alcoholic extract; Damasco and Lemonica (1999), who used an ethanolic extract). Moreover, the authors neglect reports on rosemary extracts and oils with evident positive pharmacological effects, also including antimutagenic effects.

For instance, according to Fahim et al. (1999), the administration of rosemary ethanolic extract (1.5 mg/g bw) to rats for 3 weeks displayed a hepatoprotective effect, using carbon tetrachloride and cyclophosphamide as hepatotoxic and mutagenic compounds, respectively. The effect was comparable to that with silymarin (used as reference compound) due to the amelioration of the liver function parameters. The effect was confirmed by histopathological examination of the liver tissue. Pretreatment of mice with rosemary oil (1.1 mg/g bw) for 7 days, followed by intraperitoneal injection of cyclophosphamide, reduced the induction of bone marrow suppression.

3. Validity of the results: According to the Community Herbal Monograph of the European Medicines Agency, EMA (2009), rosemary oil is made from rosemary leaves - not from complete aerial parts. It is used orally for symptomatic relief of dyspepsia and mild spasmodic disorders of the gastrointestinal tract. The recommended oral dose is 2 drops per day, which means about 60 mg rosemary oil per day. For a patient of 60 kg, the maximum daily therapeutic dose of rosemary essential oil amounts to 1.0 mg/kg bw. Therefore, it is not reasonable to test rosemary oil in doses of 300, 1000 and 3000 mg/kg bw, as was done in the Maistro and co-workers' study. Furthermore, their arguments for choosing such high doses are obscure (see Gaiani et al., 2006; they used a hydro-alcoholic extract of rosemary, not the oil) and not based on commonly accepted therapeutic recommendations (see Faria, 2005; Master's thesis). In view of this background, it is beyond our comprehension why lower doses of rosemary oil were not tested. Furthermore, the results of the genotoxicity tests did not show any dose-dependency. If so, the question about the validity of the results arises. However, the authors did not discuss this fact.

4. Conclusion of the abstract: The conclusion "that rosemary essential oil provokes genotoxic and mutagenic effects when administered orally" is by far too general, as only very high doses were used, which are never reached in the therapeutic situation, and as it was not proven that the oil they used is chemically identical to the oil used for treatment.

With kind regards, Prof. Dr. Jürgen Reichling and co-authors.

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