Mentha aquatica L. extract effects on mitochondrial bioenergetics

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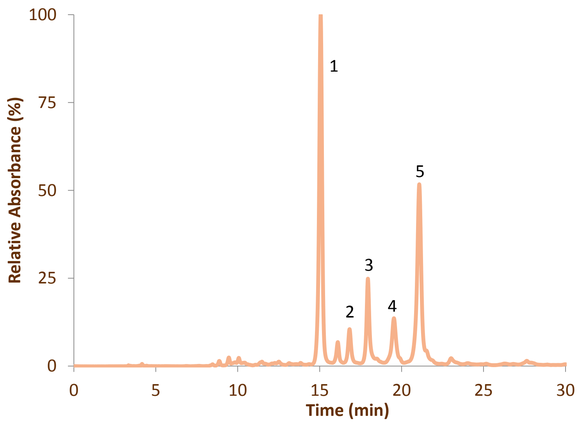
Background:

- ✓ *Mentha aquatica* L. (water mint), a Lamiaceae, is a perennial herb common in marshes and damp places from the South-western Cape to tropical Africa, where is used as a **sedative** and **anticonvulsant**;
- ✓ Due to its strong odor and particular taste, *Mentha aquatica* L. is used in **food processing**, to flavor beverages, **ice-creams** and **candies**;
- ✓ Despite its wide traditional use, no toxicological assessment of this plant has been performed.

Results

Polyphenols characterization



Peak	RT (min)	λ_{max}	[M-H]⁻	Main fragment ESI MS^n	Compound	mg/g of extract[a]
1	15.0	283, 325	595	MS^2 [595]: 287; MS^3: [287]: 269(3%), 151(100%), 125(2%), 107(1%); MS^4 [151]: 107	Eriodictyol-*O*-rutinoside	144.6 ± 22.4 (48%)
			593 (100%)	MS^2 [593]: 285 (100%), 267(10%), 241(3%); MS^3: [285]: 241 (100%), 217 (67%), 199 (65%), 175 (62%), 151(20%)	Luteolin-7-*O*-rutinoside	43.3 ± 10.0 (14%)
2	16.8	254, 267, 345	609 (35%)	MS^2 [609]: 343 (5%), 301(100%), 255 (2%), 271 (2%), 179 (2%); MS^3 [301]: 273 (10%), 257 (10%), 179 (100%), 151 (60%)	Rutin	
			449 (40%)	MS^2 [449]: 287; MS^3 [287]: 151	Eriodictyol-7-*O*-glucoside	
		254,267, 350	447 (15%)	MS^2 [447]: 285; MS^3 [285]: 243(50%), 241(100%), 217(90%), 201(7%), 199(85%), 175(75%)	Luteolin-7-*O*-glucoside	
3	17.9		461 (40%)	MS^2 [461]: 285	Luteolin-*O*-glucuronide	
		282, 333	579 (100%)	MS^2 [579]: 271; MS^3: [271]: 177(5%), 151(100%)	Naringenin-7-*O*-rutinoside	24.4 ± 3.7 (8%)
		266, 336	577 (50%)	MS^2 [577]: 269; MS^3: [269]: 241(10%), 225(100%), 224(60%), 203(30%), 183(10%), 182(20%), 151(35%)	Apigenin-7-*O*-rutinoside	
4	19.5	283, 325	609 (100%)	MS^2 [609]: 301(100), 286(<1), 242(<1); MS^2 [301]: 286(100%), 283(40%), 257(25%), 242(40%), 233(3%), 199(5%), 125(10%); MS^4 [286]: 268(5%), 258(75%), 242(100%), 199(5%), 174(5%); MS^5 [241]: 227(100%), 199(60%)	Hesperetin-7-*O*-rutinoside	25.9 ± 3.6 (9%)
		253, 267, 345	461 (40%)	MS^2 [461]: 285; MS^3 [285]: 243(20%), 241(90%), 217(45%), 199(10%), 175 (100%), 133 (14%)	Luteolin-7-*O*-glucuronide	
5	21.1	290, 328	359	MS^2 [359]: 315(2%), 223(10%), 197(15%), 179(20%), 161(100%), 133(1%); MS^3 [179]: 135	Rosmarinic acid	64.2 ± 8.8 (21%)
					Total	302.5 ± 28.7

Identification and quantification of phenolic compounds. The identification of the phenolic constituents of the purified ethanolic plant extracts was carried out by the combination of HPLC-DAD and ESI-MS^n data.

✍ **Main polyphenols of *Mentha aquatica* extract:**

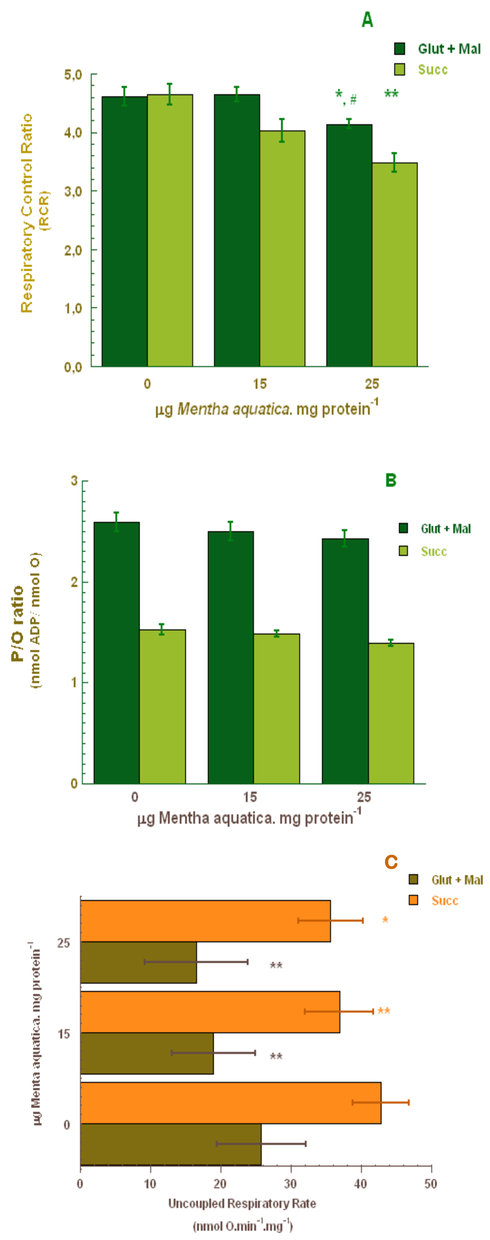
- **Eriodictyol-*O*-rutinoside** (identified as the major flavanone in *M. aquatica* accounting for almost 50% of the total quantified phenolics);
- Phenolic acid **rosmarinic acid** (64.2 ± 8.8 mg/g of extract)
- Flavone **luteolin-7-*O*-rutinoside** (43.3 ± 10.0 mg/g of extract);
- Flavanone **naringenin-7-*O*-rutinoside** (24.4 ± 3.7 mg/g of extract);
- Bioflavonol **hesperitin-7-*O*-rutinoside** (25.9 ± 3.6 mg/g of extract).

Membrane potential & Respiratory indexes

Mitochondrial membrane potential variations induced by the purified ethanolic extract of *M. aquatica:*

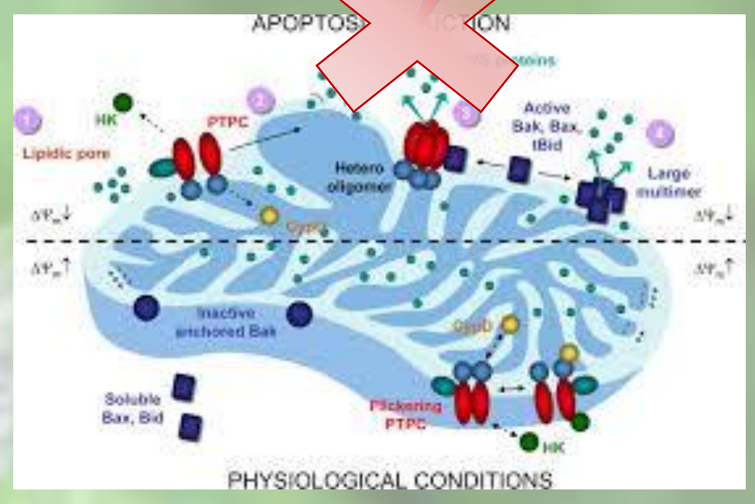
Condition	Energization (mV)	ΔADP (mV)	Repolarization (mV)	Repolarization rate (% of mean control)	Lag Phase (s)
Glutamate + Malate					
Control	209.3 ± 1.5	26.9 ± 2.0	205.7 ± 1.2	100.0 ± 6.	46.7 ± 1.2
PEE 15 µg.mg protein^{-1}	202.9 ± 2.3	27.1 ± 2.1	200.3 ± 2.4 *	84.8 ± 5.0	55.5 ± 1.0*
PEE 25 µg.mg protein^{-1}	200.8 ± 2.4*	25.8 ± 1.4	199.9 ± 1.3 *	75.5 ± 5.2 *	65.5 ± 3.2**
Succinate					
Control	218.8 ± 1.0	29.0 ± 1.1	218.4 ± 1.1	100.0 ± 5.7	66.6 ± 5.1
PEE 15 µg.mg protein^{-1}	218.3 ± 0.9	28.5 ± 2.4	216.7 ± 1.6	91.4 ± 4.3	64.0 ± 6.6
PEE 25 µg.mg protein^{-1}	215.0 ± 1.2*	27.9 ± 1.3	214.1 ± 1.4 *	75.7 ± 3.4 **	76.6 ± 5.0*

Statistics:* p< 0.05; ** p< 0.01, compared to control.



Statistics:* p< 0.05; ** p< 0.01, compared to control; # p< 0.05 compared to 15 µg Mentha aquatica L.

No effect over MPTP induction



✍ Mitochondrial parameters, RCR and uncoupled respiration are significantly decreased by *Mentha aquatica* ethanolic extract, either in the presence of glutamate + malate or succinate, as respiratory substrates, in the range of concentrations used (up to 25 µg plant extract per mg protein) → mitochondrial dysfunction, affecting respiratory chain

📚 **In conclusion, the present study suggests that a high daily consumption of (ethanolic) extract of *M. aquatica* leaves, as a nutraceutical, should be regarded as hazardous due to its chemical composition and effects on mitochondrial OXPHOS.**

Nevertheless, the mild mitochondrial stress induced by the polyphenols present in *M. aquatica* extract, at lower dosages act as hormetic stimuli and can account for the antioxidant and anti-inflammatory properties of *M. aquatica* observed *in vivo* [1] and contribute to a higher mitochondrial flexibility [2].

References:

1. Conforti, F., Sosa, S., Marrelli, M., Menichini, F., Statti, G. A., Uzunov, D., Tubaro, A., Menichini, F., and Loggia, R. D. (2008) *J. Ethnopharmacol. 116*, 144-151.
2. Nunn, A., Bell, J., and Guy, G. (2009) *Nutr. Metabol. 6*, 16.

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