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Editorial

Analgesic Resveratrol?

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ABSTRACT

Resveratrol, a red wine and grape-derived phytoalexin, possesses diverse biochemical and physiological functions that are relevant to human health and disease. The emergent properties of resveratrol have forced us to rethink the biomedical significance of the wine culture. Novel observations point to the hypothesis that intracerebral resveratrol treatment diminishes the sensitivity of rats to pain, and that the said analgesic action of resveratrol is a central mechanism mediated by the inhibition of cycloxygenases I and II. This novel implication of resveratrol and perhaps red wine drinking warrants further studies. *Antioxid. Redox Signal.* 10, 403–404.

Resveratrol, a red wine and grape-derived phytoalexin, possesses diverse biochemical and physiological actions, including estrogenic, antiplatelet, and anti-inflammatory properties. It has been found to prevent prostate, pancreatic and thyroid cancer, UV radiation injury, cerebral ischemic injury, growth of *H. pylori*, herpes simplex virus types 1 and 2 replication, DNA damage, apoptosis, and LDL oxidation (1). Other health benefits of resveratrol include chemoprevention, cardioprotection, neuroprotection, and anti-aging action (1). Although anti-inflammatory activity of resveratrol has been extensively studied, its analgesic effects, which usually accompany anti-inflammatory effects, have received much less attention. Recently, we studied the analgesic effects of resveratrol in rats by the Tail-Flick method (2). The results show that resveratrol functions as potent analgesia.

As shown in Table 1, treatment with resveratrol doubled the time to response to pain as determined by the Tail-Flick test. Irrespective of the mode of treatment, resveratrol dose-dependently showed potent analgesic effect. Representative figures shown in Figure 1 reveal inhibition of both COX I and COX II mRNAs [A] and proteins [B] by resveratrol at a dose (5 mg/kg) that doubled the time to response to pain. The enzyme activities determined by estimating PGE_2 formation was also inhibited by resveratrol [C]. Thus, intracerebral resveratrol

Table 1. Evaluation of Analgesic Effect of Resveratrol

Treatment	*Mode of treatment*	*Dose (mg/kg)*	*Time of analgesic reaction/sec*
Control			3.5
Resveratrol	Oral	2.5	7.5
	Oral	5.0	9.0
	i.p.	2.5	3.0
	i.p.	5.0	11.0

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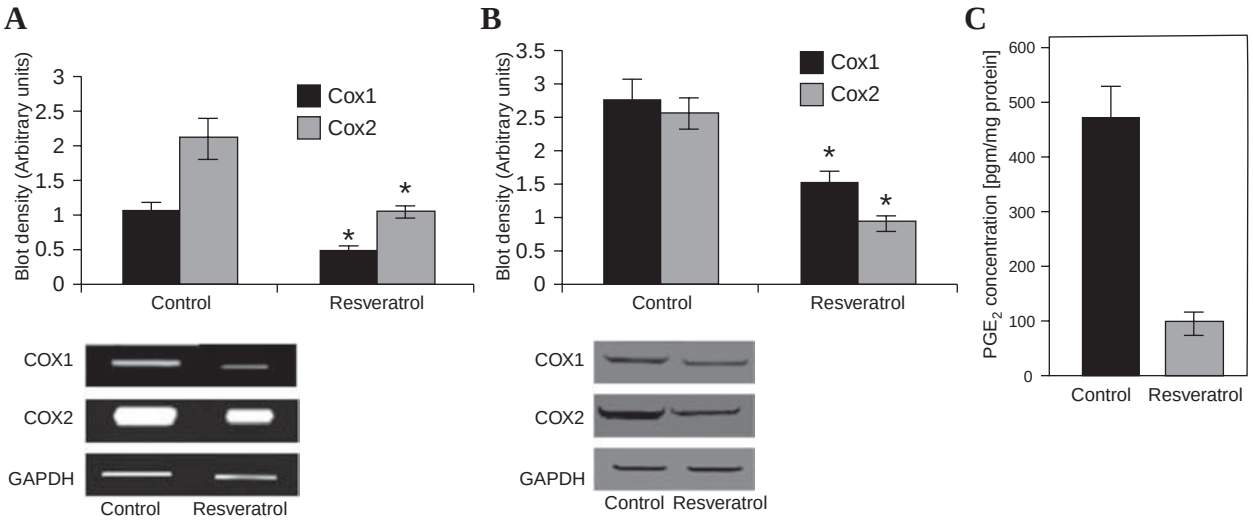

FIG. 1. Effects of resveratrol on the inhibition of the expression of COX I and COX II genes (A), proteins (B), and enzyme activity (C). Experiments were performed as described in the Methods. The mRNAs of COX I and COX II were determined using RT-PCR technique while the proteins were determined by Western blot analysis. The enzyme activity was assessed by determining PGE_2 formation by ELISA. The blots are shown as representative of three separate experiments, and bar graphs are the means ± SEM of three experiments. $*p < 0.05$ vs. control.

treatment diminished the sensitivity of rats to pain, indicating that analgesic action of resveratrol is a central mechanism mediated by the inhibition of COX I and COX II.

APPENDIX

Laboratory rats treated according to the regulations of European Community [86/6009/EC)] as well as NIH guidelines (NIH 85-23), were properly anesthetized with sodium pentobarbital. A cannula was implanted stereotaxically into the lateral ventricle of the brain. After 2 weeks, angiotensin IIa (0.2 mg/ml saline) was injected to verify that the implant was in the correct position. The animals were then divided into two groups–-one group received resveratrol injected into the cerebral ventricles, while the other group received vehicles only. Reaction to pain was assessed by measuring the time to tail flick following pain induced by heat (Tail-Flick test) (2). To examine if the analgesic action is linked with Cox inhibition, Cox I and Cox II activities were analyzed in the brain by both RT-PCR for mRNA, and Western blot analysis for protein expression, while enzyme activity was determined by estimating the amount of prostaglandin E2 (PGE_2).

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ABBREVIATIONS

Cox I, cyclooxygenase 1; Cox II, cyclooxygenase 2; ELISA, enzyme-linked immunosorbent assay; LDL, low-density lipoprotein; RT–PCR, reverse transcription polymerase chain reaction; UV, ultraviolet.

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