Warfarin resistance: interaction between warfarin and Eruca sativa L.

Mustafa Goz[a], *Fugen Goz*[b], *Omer Cakir*[a], *Belkis Aydinol*[c], *Nesimi Eren*[a]

[a] Dicle University School of Medicine, Department of Cardiovascular Surgery,
[b] Dicle University Health School, Diyarbakir, Turkey
[c] Department of Biochemistry

Warfarin is effective in the prevention and treatment of venous and arterial thrombosis. Eruca sativa (Arugula, roquette, rocket salad)[1] is native to western Asia and the Mediterranean region. It is standard table fare in Italy, the south of France, Turkey and Greece. Eruca sativa is a plant that can be consumed in salads and used in herbal treatments. It contains 130 µg of vitamin K per 100 g [1] (table 1).

In this paper, we present the phenomenon of warfarin resistance developing due to roquette intake, highlighting the warfarin-food interaction.

A 52-year-old woman with venous thromboembolism (left limb acute proximal deep venous thrombosis) had been receiving warfarin therapy since September 2004. INR levels with a dose of 7.5 mg/day of warfarin (target range 2.5–3) continued at therapeutic levels until December 2004. In the INR check carried out after this date, it was determined that the warfarin treatment was no longer effective. The patient was hospitalised. She was tested by gradually increasing the dose of warfarin to 20 mg/day. However, there was no increase in the value of INR. She had no history of drug or food intake that could have caused a warfarin interaction. However, within the previous two weeks the patient had tried herbal medicines and had consumed a lot of Eruca sativa daily. Because Eruca sativa contains high levels of vitamin K, further intake was stopped. During this period, DMAH prophylaxis was used. Then warfarin treatment with a dose of 5 mg/day was started again. Three days later her INR value was determined to be 2.1. In the 3-month follow-up, INR was observed to continue at the therapeutic level with warfarin treatment of 7.5 mg/day (figure 1).

The increasing use of warfarin requires that more attention be paid to drug intake and food regimes. The drug and food interactions observed can cause bleeding and thromboembolism that can be life-threatning. There is sufficient information on drug interactions of warfarin in the literature [2, 3]. However, there is not enough information on food interactions. In addition, Couris et al. [4] indicated that professional health workers do not have enough information on this subject.

Dietary intake of vitamin K is important. However, a dose-response effect of vitamin K on warfarin anti-coagulation has not yet been established. There are sufficient data to suggest that a constant dietary intake of vitamin K that meets current dietary recommendation of 65–80 µg/day is the most acceptable practice for patients on warfarin therapy [5].

Eruca sativa is native to western Asia and the Mediterranean region. It is commonly known as "rucola" in Italy, "ackerrauka" in Germany and kibana-suzushiro' in Japan. It is an annual herbaceous plant belonging to the family Brassicaceae. Because of its high content of glucosinolate, it is an effective antioxidant [6]. Eruca sativa is used as an appetizer, blood cleaner, sexual power enhancer, and urine and phlegm discharger. However, it contains 130 µg of vitamin K per 100 g [1]. In patients using warfarin, an increase in levels of vitamin K can lead to warfarin resistance if care is not taken. The literature does not appear to contain any information on an interaction between warfarin and Eruca sativa.

As reported here, a large intake of Eruca sativa during warfarin treatment can cause acquired, temporary warfarin resistance, due to its high vitamin K content. In a study by Booth et al. [5], it was stated that warfarin resistance could result from eating dark green foods (broccoli, Brussels sprouts, collards, spinach and coleslaw) with high phylloquinone content (vitamin K). Furthermore, herbal teas (Lycium barbarum L.) and multivitamin preparations can cause a drug-food interaction by the same mechanism [7–9].

Table 1

Vitamin content of Eruca Sativa L.

Vitamin	µg/100 gr
A	240
D	0
E	60
K	130
B_1	60
B_2	80
B_6	60
Niacin	320
Biotin	1.9
B_{12}	0
C	13 000

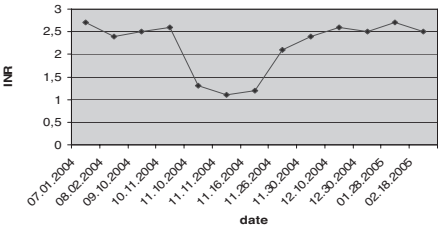

Figure 1

INR values of the patient.

In conclusion, healthy nutrition and the desire to live longer increase the tendency to try herbal treatments. This brings potential dangers. As seen in the case we have reported, in patients that are treated with drugs that have serious drug and food interactions, such as warfarin, life-threatening results can be seen. Therefore, we think that patients on warfarin should be better informed about drug-food interactions.

Correspondence:
Dr. Mustafa Goz
Dicle Universitesi
Tip Fakultesi
Kalp ve Damar Cerrahi AD
21180-Diyarbakir
Turkey
E-Mail: mustafagoz@dicle.edu.tr

1 In Switzerland: Rucola salad

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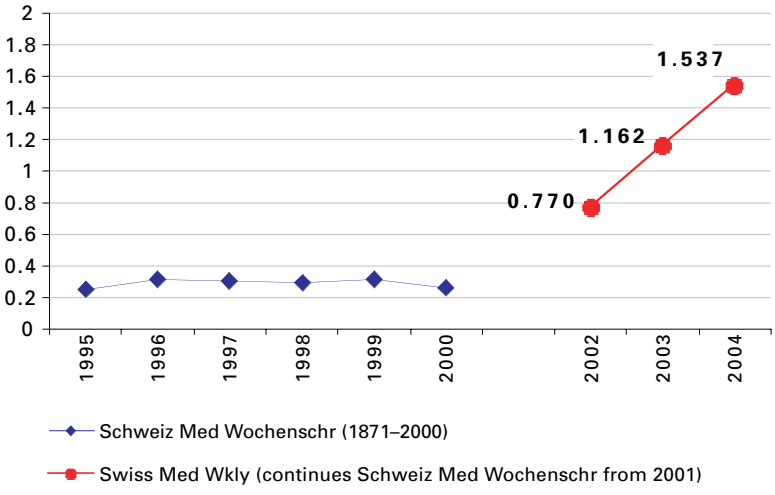

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