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Clinical Effect of Buckwheat Herb, *Ruscus* Extract and Troxerutin on Retinopathy and Lipids in Diabetic Patients

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In this study the effect of a buckwheat herb and a *Ruscus* extract preparation, compared with troxerutin, are described with respect to ophthalmological and biochemical parameters in patients with non-proliferative diabetic retinopathy. During the study period of 3 months, 60 diabetic patients were divided into three equal groups: in group I troxerutin was given, in group II *Ruscus* extract and in group III buckwheat herb was administered. At the beginning and on the last day of the study, each patient was subjected to ophthalmological and clinical biochemistry. The amplitude of oscillating potentials was decreased in patients receiving troxerutin, but increased in group II and group III. Regression of changes located in the fundus of the eye was demonstrated in 23.1%–27.8% of all treated patients, however deterioration in 5.6% of patients given troxerutin and in 3.3% of subjects treated with buckwheat herb was observed at the same time. No cases with progression of abnormalities in the fundus of the eye were found in group II. Moreover, troxerutin seemed to be less effective, especially when oscillating potentials were concerned. The use of buckwheat herb for the prophylaxis and treatment of diabetic patients, suffering from retinopathy is recommended.

Keywords: buckwheat herb and *Ruscus* extract; diabetic retinopathy; carbohydrates and lipids.

INTRODUCTION

Microangiopathic complications of diabetes, among them diabetic retinopathy, occur in a considerable number of subjects affected by the disease. In patients with overt diabetes for 5 years, the incidence of retinopathy averages 30%, and it increases to 60% and 70%–80% after 10 and 15 years of the disease and may result in total blindness. In the early stages of the disease, advanced changes in diabetic retinopathy may not be diagnosed due to small incidence of vision disturbances, so that patients are often presented with abrupt deterioration of vision. Early detection of diabetic retinopathy as well as the introduction of proper medication may retard the progress of disease.

Electroretinography can be a useful tool for the early diagnosis as well as prognosis of certain diseases of the retina and of the optic pathway. Oscillating potentials are recorded during electroretinographic examination. They were described for the first time by Cobb and Morton (1953). In humans up to 4–5 waves of oscillating potentials can be usually detected. Heck and Rendahl (1957) reported four peaks of varying appearance related to frequency of stimulation. Each wave, from 0_1 to 0_4, is characterized by a latent period (latency time), amplitude, duration and cumulation time.

The investigation was aimed at evaluating medication with *Ruscus* extract and buckwheat herb compared with troxerutin regarding ophthalmological findings, course of diabetes and lipid profile, following a 3-month period of treatment in patients suffering from diabetes mellitus.

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MATERIAL AND METHODS

The study was carried out with 60 individuals (32 women, 28 men), aged 20–75 years, mostly suffering from non-insulin dependent diabetes mellitus (type II) for 1–27 years, characterized by non-proliferative diabetic retinopathy. They were randomly assigned to three equal groups: group I - treated with troxerutin, group II - under *Ruscus* medication, and group III - on buckwheat herb. Diseases of the kidney and the liver, allergy, venous abnormalities as well as psychosis were exclusion criteria. The study protocol was approved by the local Ethics Committee, and each patient gave written informed consent. During the study period of 3 months, all subjects remained on a stable diabetic diet, unchanged hypoglycaemic medication for the period of treatment and were additionally given: group II - troxerutin (Venoruton Zyma, GmbH) 1 tablet containing 0.5 g of 0-(beta-hydroxyethyl)-rutoside), 2 times a day; group III - 1 capsule of *Ruscus* (botanical name: *Ruscus aculeatus* Linne) extract (Fagorutin-Ruscus, Fink GmbH), containing 0.0375 g of the extract from butchers broom 2 times a day; and group III - 2 tablets of pressed buckwheat herb (botanical name: *Fagopyrum esculentum* MOENCH) 3 times a day (Fagorutin Buchweizen Tabl., Fink GmbH; 1 tablet contains 0.5 g *Fagopyrum esculentum* herb and 0.03 troxerutin). Any hypolipaemic medication, if administered earlier, was withdrawn at least 4 weeks before the onset of the study.

At the beginning, as well as on the last day of the investigation each patient was subjected to an ophthalmological examination which included: visual acuity (vision test chart), examination of the anterior segment of the eyeball (slit lamp) as well as the fundus of the eye (ophthalmoscope), and static perimetry (automatic perime-

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Table 1. Mean (±SE) values of oscillating potentials (μU) at the onset of the study (A) and after 3-month medication (B)

Group	Eye	Oscillating potentials $\Sigma 0_1+0_2+0_3$ A	B	A-B (Difference)	Statistical significance (*p*) A/B
I	Right	67.9±13.4	53.6±3.8	−14.3±11.9	>0.4
(Troxerutin)	Left	58.2±7.9	42.7±5.2	−15.5±5.2	>0.1
II	Right	56.1±4.1	65.8±9.0	9.7±6.7	>0.1
(*Ruscus* extract)	Left	60.7±5.4	68.5±9.5	7.8±6.7	>0.4
III	Right	75.5±9.1	79.9±9.9	4.4±13.0	>0.4
(Buckwheat herb)	Left	66.2±8.5	86.9±11.6	20.8±13.9	>0.1

ter, Tübinger type TAP 2000 cc, Oculus). The oscillating potentials of the electroretinogram were also recorded. After a 3-month period of treatment, based on the picture of the eye fundus, examination results were classified as follows: (a) deterioration (an increase in aneurysmatic changes, indurate exudates and petechias) compared with the initial findings, (b) improvement (a decrease in the above mentioned symptoms), (c) no changes.

Electroretinography was performed twice on scheduled days, using a computer device for electrophysiological examinations type UTAS-E (SA Universo, La-Chaux-deFonds, Switzerland). Amplitudes of oscillating waves ($0_1+0_2+0_3$) were determined.

In the blood serum the following biochemical parameters, at the beginning and at the end of the investigation, were determined: total cholesterol, HDL-cholesterol and triglycerides using Boehringer Mannheim GmbH kits, fructosamine (Fructosamin-Test, Roche), glycosylated haemoglobin (Abbott), and glucose by Trinder (1969).

The results were statistically evaluated using Student's *t*-test. A value of $p<0.05$ was considered significant.

RESULTS

Group I, medicated with troxerutin, was characterized by a decrease in amplitude of oscillating potentials by 21%, considering both eyes (Table 1). In contrast, in group II and group III, treated with *Ruscus* and buckwheat herb, an increase in amplitude of oscillating potentials (by 15% and by 18%, respectively) was observed. The changes in the amplitude detected were statistically insignificant when compared with the initial values.

In all patients treated for 3 months with troxerutin, *Ruscus* and buckwheat herb preparations, a slight, statistically insignificant increase in visual acuity was observed: from 0.82 to 0.91 in group I, 0.83 to 0.93 in group II, and 0.97 to 0.98 in group III.

Examination of the anterior segment of the eyeball after 3 months of pharmacotherapy did not show any differences when compared with the initial picture in all the groups evaluated.

A regression of changes located in fundus of the eye was demonstrated in 27.8% while a progression in 5.6% of patients treated with troxerutin was observed. Evaluation of the fundus of the eye in group II (*Ruscus*) revealed a quite distinct improvement in 23.1% of patients and no cases with progression, while in patients receiving buckwheat herb (group III) an improvement was demonstrated in 26.7% and a deterioration in 3.3% of the examined diabetics.

Static perimetry revealed a decrease by +2.6 dB in group I, +0.8 dB in group II, and +2.5 dB in group III, of mean intensity of defect (loss) in vision area after 3 months of medication.

The results of glucose, fructosamine and glycosylated haemoglobin concentrations are outlined in Table 2. Mean blood serum concentrations of glucose decreased by 12.7% in the troxerutin treated group ($p<0.001$), in the *Ruscus* group by 10.6% ($p<0.01$), and in subjects medicated with buckwheat herb by 15.1% ($p<0.001$). Similarly, concentrations of fructosamine and glycosylated haemoglobin were lower after the 3-month period of treatment in all groups studied.

Blood serum concentrations of fructosamine and glycosylated haemoglobin were decreased in group II by 7.8% ($p<0.01$) and 15.6% ($p<0.001$) and in group III by 11.9% ($p<0.05$) and 3.3% ($p<0.01$), respectively. Significant changes were also noted in blood serum concentrations of total cholesterol and HDL-cholesterol (Table 3). In all study groups total cholesterol dropped: in group I by 7.6% ($p<0.001$), in group II by 9.4% ($p<0.01$) and in group III by 14.9% ($p<0.001$), whereas HDL-cholesterol increased in these groups by 41% ($p<0.001$), by 23% ($p<0.001$), and by 13% ($p<0.0001$), respectively.

DISCUSSION

The feasibility of using oscillating potentials in the diagnosis of vascular diseases is entirely warranted. Korol

Table 2. Mean (±SE) values of biochemical parameters at the onset of the study (A) and after 3 months of treatment (B)

Group	Glucose (mmol/L) A	B	*p*	Fructosamine (mmol)L) A	B	*p*	Glycosylated haemoglobin (%) A	B	*p*
I	10.9±0.8	9.5±0.7		3.35	3.26		6.78	6.19	
(Troxerutin)			<0.001	±0.15	±0.14	<0.05	±0.49	±0.50	<0.01
II	10.4±0.8	9.3±0.7		3.26	3.01		6.27	5.29	
(*Ruscus* extract)			<0.005	±0.14	±0.10	<0.01	±0.30	±0.18	<0.001
III	10.3±0.8	8.7±0.7		3.28	2.89		6.34	6.13	
(Buckwheat herb)			<0.001	±0.19	±0.10	<0.05	±0.40	±0.37	<0.01

p, statistical significance.

Table 3. Mean (±SE) lipid concentration in the blood serum prior (A) and after 3 months of treatment (B), including statistical significance (*p*)

Group	Total cholesterol (mmol/L)			Triglycerides (mmol/L)			HDL-cholesterol (mmol/L)		
	A	B	*p*	A	B	*p*	A	B	*p*
I (Troxerutin)	5.1±0.4	4.7±0.4	<0.001	1.29 ±0.12	1.21 ±0.09	>0.1	0.89 ±0.09	1.26 ±0.09	<0.001
II (*Ruscus* extract)	5.8±0.3	5.2±0.2	<0.005	1.62 ±0.2	1.52 ±0.19	>0.2	1.07 ±0.08	1.31 ±0.08	<0.001
III (Buckwheat herb)	5.7±0.3	4.9±0.2	<0.001	1.64 ±0.24	1.36 ±0.24	<0.01	1.16 ±0.08	1.32 ±0.08	<0.001

(1973) and Korol *et al.* (1975) in studies with glycine as an inhibitor of neurotransmission in the central nervous system (also in the retina) showed that their source are the amacrine cells lodged in the granular layer of the external retina, and are supplied by central arterial rammifications. These cells are involved in the modulation of visual stimuli in the retina, participating in the transmission of neural stimuli. They undergo depolarization when excited by bipolar cells. Rapid displacement of ions is a high energy-consuming process. Disturbances in blood supply, leading to defects in the proper transport of high-energy materials, are found to cause functional deficiencies in amacrine cells, which is reflected in the reduction of the amplitude of oscillating potentials. Simonsen (1966, 1980) demonstrated great predictive value of the measurement of oscillatory potentials in diabetic patients in selecting those at risk of developing proliferative retinopathy, except for women who later became pregnant. In the present study we observed a rise in the amplitude of oscillatory potentials in subjects treated with *Ruscus* and buckwheat herb, which may suggest an improvement in local blood circulation in the retina, i.e. a regression in the development of diabetic retinopathy. The differences, although not significant, show a beneficial influence of the above remedies, and are to be proven in a greater number of cases. Both *Ruscus* and buckwheat herb demonstrate an advantage when compared with troxerutin alone, a drug with established efficacy in vasculopathies. Profitable effects of the drugs examined on the course of diabetic retinopathy were confirmed by ophthalmological examination. In the group maintained for 3 months on *Rucus* treatment regression of the diabetic retinopathy was detected in 23.1% of patients with no cases of disease progression. However, 27.8% of patients treated with troxerutin showed regression and 5.8% displayed progression of diabetic changes within the fundus of the eye. Administration of buckwheat herb resulted in the regression of signs of diabetic retinopathy in 26.7% of patients, whereas progression was observed only in 3.3%. So, in all study groups similar effects of the drugs were shown, as examined by ophthalmoscopy. It seems that the measurement of oscillating potentials may be a more sensitive method than ophthalmoscopy in the diagnosis of progression of diabetic changes in the fundus of the eye. Since most of the patients did not show metabolic dysregulation at the time of the study, and remained on a stable diet and hypoglycaemic medication, the observed changes in biochemical parameters could be ascribed to the properties of the administered drugs.

The most pronounced, statistically significant, decrease in blood serum level of fructosamine and glycosylated haemoglobin was observed in the *Ruscus* and buckwheat herb treated groups. Significant changes were also noted in the blood serum concentrations of total cholesterol and HDL-cholesterol. In all groups of the study blood serum cholesterol as well as glucose levels were decreased. The above mentioned changes may reflect a hypoglycaemic activity of troxerutin, *Ruscus*, and buckwheat herb or an increased response to hypoglycaemic treatment.

Fagopyrum esculentum buckwheat herb is a source for the industrial extraction of rutin (Moumou and Trotin, 1992), a compound which is applied to improve capillary fragility. The present study confirmed the beneficial effects of buckwheat herb (*Fagopyrum esculentum*) in the development of diabetic retinopathy. A 3-month period of treatment resulted in the regression of the changes located in the fundus of the eye, in a considerable fraction of patients, and an increase in the amplitude of oscillating potentials. The drugs containing buckwheat herb and butchers broom showed superiority compared with 0-(beta-hydroxyethyl)-rutoside. The profitable influence of *Fagopyrum esculentum*, and additionally troxerutin on the course of diabetic retinopathy may be the result of its antioxidant properties, which is in keeping with observations of Wójcicki *et al.* (1995). It was shown earlier that naturally occurring bioflavonoids have antioxidant and membrane stabilizing properties and an ability to scavenge free radicals (Das and Sothy, 1971). A further advantage of the drug containing *Fagopyrum esculentum* may be the amelioration of lipid metabolism disturbances, confirming the data supplied by Bijlani *et al.* (1985) and Wójcicki *et al.* (1995). During the study the authors observed a profitable effect of the drugs based on buckwheat on glucose tolerance and on the lipid metabolism disturbances. Thus, we can conclude that buckwheat herb may be an effective agent in the prevention and treatment of diabetic retinopathy.

Our investigation revealed the superiority of buckwheat herb containing remedies compared with troxerutin alone, a rutoside derivative.

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