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Oral therapy with proteolytic enzymes: Effects on hemorheological parameters

E. Ernst

Postgraduate Medical School, University of Exeter, Exeter, UK

Summary

In the course of a randomized, double-blind, cross-over study, 10 healthy volunteers received a daily oral dosage of 30 coated Wobenzym® tablets (a mixture of proteolytic enzymes) or a placebo for two weeks. A quantification of the complete hemorheological profile served as the primary endpoint. No changes were observed in the placebo group for any of the measured variables. Under medication with the active preparation, however, a decrease in blood and plasma viscosity, erythrocyte rigidity and erythrocyte aggregation could be observed. The parameters of the blood count, serum electrophoresis and colloid osmotic pressures were unaltered under therapy with either the placebo or Wobenzym®. No adverse drug reactions were observed with either the placebo or the active medication. It is concluded that the oral application of Wobenzym® significantly changes the flow properties of blood in healthy volunteers. Further clinical trials must be performed in order to determine whether these effects can be employed for improving blood perfusion, for instance in the event of ischemic disease.

Keywords: proteolytic enzymes, hemorheology, complementary medicine

The therapeutic influence of disturbed blood flow properties is a promising procedure in principle, especially for the treatment of patients with arterial ischemia. For such treatment a number of preparations are available for oral application today (2). The hemorheological effects of proteolytic enzymes are under-investigated thus far. They may result in a modification in blood flow characteristics as a result of the degradation of rheologically effective macromolecules which are present in the plasma (e.g. fibrinogen). This hypothesis is to be investigated with the aid of a double-blind study performed on healthy volunteers. The enzymes were administered orally, a process which, according to the teaching of orthodox medicine, should result in no systemic alterations.

Test subjects and methods

Ten clinically healthy volunteers demonstrating no pathological alterations in routine laboratory findings, whose clinical and anamnestic findings were nor-

mal, who were not taking any medications at the beginning of the study, gave their consent to take part in this investigation. They received a daily dosage of 30 Wobenzym® or placebo tablets orally over a period of two weeks. The study was randomized, double-blind and was carried out in a cross-over design. The wash-out phase between the phases with the active drug or the placebo lasted one week.

A tablet of Wobenzym® contains 100 mg of pancreatin, 45 mg bromelain, 60 mg papain, 10 mg triacylglycerol lipase, 10 mg amylase, 24 mg trypsin, 1 mg chymotrypsin and 50 mg of rutoside.

During each period of the study, venous blood samples were taken before, and after both one and two weeks of routine medication, and the following parameters were measured:

1. Native, whole-blood viscosity at 37 °C and at three defined shear rates in an LS-30 rotation viscosimeter (Contraves) (7, 10),
2. viscosity of whole blood as above, but standardized to a hematocrit of 45 l/l (8),

3. plasma and serum viscosity at 37 °C (6),
4. hematocrit (5),
5. erythrocyte flexibility with a nucleopore (5 µm) filtration method, as well as
6. erythrocyte aggregation (Myrene) (9).
7. The compliance was quantified by a „pill" count.

The evaluation of the data was carried out with the non-parametric Wilcoxon test and with the Wilcoxon tests for paired and unpaired data. After verifying that no residual effects were present, the results for the phases with the actual drug and with the placebo were pooled and evaluated regardless of their sequence. The null hypothesis was rejected if p was less than 0.05.

Results

The data reveal that the compliance of all subjects was optimal. Under placebo, none of the examination parameters revealed any significant differences. After two weeks of therapy with Wobenzym®, however, a reduction in the blood viscosity was found which was independent of the hematocrit. The serum and plasma viscosity under Wobenzym® demonstrated significant decreases even one week after the beginning of therapy. Furthermore, the erythrocyte aggregation and erythrocyte flexibility yielded significant differences in the sense of an improvement in blood flow properties (Table 1).

Discussion

The results show that the oral administration of Wobenzym® in healthy individuals leads to significant changes in the flow properties of blood. Our group was also able to demonstrate similar changes in a group of patients suffering from rheumatoid arthritis, although a prepara-

Table 1: Hemorheological alterations (in % of the initial values) during treatment with Wobenzym® (mean values ± 1 standard deviation)

Parameters [dimensions]	Active drug			Placebo			
	Initial values	After 1 week	After 2 weeks	Initial values	After 1 week	After 2 weeks	
Whole blood viscosity [mPas]	94.5 l/s* 2.4 l/s* 0.7 l/s*	4.6±0.7 14.8±4.4 25.2±7.5	4.3±0.4 13.4±3.9 22.4±6.8	4.3±0.4 13.5±3.6 21.0±5.3 (a/b)	4.7±0.7 14.9±4.0 25.3±6.6	4.6±0.5 14.5±4.6 24.3±6.9	4.5±0.4 13.9±3.4 23.8±5.2
Whole blood viscosity [mPas] at 45 l/l HCT	94.5 l/s* 2.4 l/s* 0.7 l/s*	4.8±0.1 15.9±2.3 27.6±4.3	4.6±0.3 14.8±1.6 25.4±2.6 (a)	4.6±0.1 (a) 14.8±1.8 23.5±2.4 (a/b)	4.8±0.1 15.4±1.0 26.9±3.2	4.8±0.2 15.3±1.8 26.8±3.9	4.8±0.2 15.4±1.8 27.4±4.0
Hematocrit [l/l]		43.3±4.3	42.9±2.9	43.9±4.1	43.4±4.1	42.9±3.6	42.9±3.2
Serum viscosity [mPas]		1.09±0.04	1.07±0.03 (a/b)	1.05±0.05 (a/b)	1.10±0.02	1.10±0.04	1.10±0.03
Plasma viscosity [mPas]		1.20±0.04	1.17±0.03 (a/b)	1.16±0.03 (a/b)	1.20±0.03	1.20±0.04	1.21±0.04
Erythrocyte aggregation [units]		12.2±4.00	10.0±3.2 (a/b)	10.1±3.2 (a/b)	11.6±3.5	12.4±4.5	12.7±3.3
Erythrocyte flexibility [units]		58±6	63±3	65±3 (a/b)	60±3	59±4	59±4

* Figures are related to shear rates in 1/s

Significant differences ($p < 0.05$):

a = as compared to the initial values

b = as compared to the values found with placebo at the same measurement time

tion without rutoside was employed (unpublished data). This implies that the enzymatic components of Wobenzym® (and not the rutoside) are responsible for the rheological effects. This in turn suggests that these enzymes are able to degrade plasma proteins in the bloodstream (e.g. fibrinogen). This mechanism, at any rate, is the most likely explanation for the hemorheological effects observed here (3). Since this hypothesis opposes the teachings of orthodox medicine, however, evidence supporting its validity must be collected in further studies. The possibility of an influence of oral enzyme therapy on the fibrinogen level is also of special importance considering the generally accepted fact that an elevated fibrinogen level represents an important, independent cardiovascular risk factor (4).

The present data provide no information as to whether or not the hemorheological effects of Wobenzym® could also be applied clinically. In principle this would be promising since hemorheological treatment is today considered to be a generally accepted therapeutic intervention, for instance in the therapy of peri-

pheral arterial occlusive disease (3). The possibility of transferring this argument by analogy to Wobenzym® must therefore be examined in suitable clinical studies performed on patients with circulatory diseases.

In summary the present data indicate that the blood flow properties of healthy subjects can be influenced positively in the sense of an increased blood fluidity through the oral administration of Wobenzym®.

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Author's address:
Prof. Dr. med. E. Ernst
University of Exeter
Postgraduate Medical School
Exeter, UK