

PART II

During a previous work we studied the effect of procyanidol oligomers on capillary permeability [5]. The study on their effect on capillary permeability appeared to us to logically complete our results.

PHYSIOLOGICAL REMINDER

Even though the capillary permeability conditions the plasmatic exudation, the capillary resistance designs a physical property of the vessels walls to oppose those forces exerting against it; forces which reach the passage, go through it with the figured elements.

The “ever pathological” shrinking of the capillary resistance will translate into an extravasation of the blood towards the tissue which becomes in diverse clinical aspects of the purpura.

Thus the capillary resistance appears to be directly linked to the anatomical state of the walls and the integrity of each constitutive element, notably that of the basal membrane [7]. We understand then the interest in the therapeutics of the substances from a trophic and stabilizing action on the conjunctive armature of the micro vessels: Capillary resistance problems are frequently observed in people with hypertension and especially in diabetics [4].

PRODUCT USED

Our work was carried out on Endotelon. This is a natural substance extracted from the ligneous tissue of the vine [10], presenting itself as a polymer with a one-molecule base, which is called procyanidol and is a vegetal polyphenol in the class of flavanols. In fact, this substance is endowed with a high vitamin P activity in a mixture of oligomers. Each molecular compound does not go beyond three or four elementary designs.

The high polymers (more than 10 elements) constitute the catechist tannins that have a stabilizing action on collagen fibers.

The pharmacological studies done on animals with the product marked with ¹⁴C showed a good digestive absorption and it's preferential adhesion on those organs rich in glycoaminoglycans, notably the vascular walls.

Other studies proved a favorable effect in those with degenerative micro-angiopathies especially those who are diabetic and have arterial hypertension.

STUDY METHOD

Capillary resistance was measured using a Lavollay “capillaro-dynamometer”, a derivative of the suction cup test. Our method consisted in creating a depression on a limited coetaneous zone for a determined amount of time. The time and pressure were

changed until the appearance of purpura. The lowest pressure number used, starting when at least three purpura appeared, determined the level of capillary resistance. The normal value is 20 cm Hg. The apparatus was made up of a small sealed chamber made out of transparent plastic forming a suction cup and linked to a manometer and a suction pump, allowing us to progressively establish the desired depression. It was applied above the elbow for one minute.

CLINICAL STUDY OF THE EFFECTS OF Endotelon

Our study was carried out on those patients whose capillary resistance was clearly below the norm and was receiving no other vascular treatment.

The controls effected in the beginning and at the end of the treatment were carried out on:

- Capillary resistance
- Renal function
- Arterial tension
- Medicine tolerance

Our study was done in two parts: An open clinical study of the effects of Endotelon and a comparative study using the double blind method using Endotelon and a placebo.

Preliminary Clinical Study

We used 28 patients (13 men and 15 women) aged from 18 to 68 years old with the average age at 46.4 years old. We attained the following:

- Nephropathy
- Arterial hypertension
- Cyclical idiopathic oedemas

Endotelon was prescribed at 2 or 3 sugar coated pills a day with the treatment lasting from one to three months. Before anything else the results were evaluated on capillary resistance by comparing the numbers before and after treatment. This remained unchanged 8 times. It increased in 18 patients.

- 2 cm Hg: 8 times
- 4 cm Hg: 5 times
- 6 cm Hg: 3 times
- 8 cm Hg: 2 times

In two instances the treatment had to be stopped early and we were unable to study the variations.

Globally capillary resistance goes from an average figure of 15.4 ± 1.8 -cm Hg before treatment to 18.1 ± 3.2 cm Hg after treatment. The comparison of these two average values shows a very significant difference ($p < 0.0005$).

Taken all together the results were more favorable with a dosage of three pills a day for at least two months. However, equally good results were obtained with a daily dosage of two pills only or after the shortest delay of the treatment.

Comparative Study In a Double Blind Using a Placebo

Two types of conditioning of strictly identical aspects were used: One contained the active ingredient, the other the placebo. Deciding who would follow which treatment was done by a lottery and no one was told who had taken what treatment until the study was concluded. We had therefore:

- 13 patients taking Endotelon
- 12 patients taking the placebo

The first series of patients was comprised of five men and eight women (average age 46.1). The second series was six men and six women (average age 47).

Capillary fragility was shown in our first study as three different types of affections:

	Endotelon	Placebo
Arterial Hypertension	6	6
Nephropathy	6	3
Cyclic Idiopathic Oedemas	1	1

The results of this study were objectified by the measure of capillary resistance retained as criteria of efficiency.

The statistical studies of the capillary resistance figures showed that:

- A highly significant increase in the average value of the capillary resistance before and after treatment with Endotelon going from 14.6 ± 0.98 cm Hg to 18.0 ± 3.35 cm Hg ($p < 0.0005$).
- An insignificant increase in the figures of those taking the placebo (14.7 ± 1.3 cm Hg in the beginning of the study and 15.5 ± 1.85 cm Hg at the end).

Moreover, the statistical comparison of the capillary resistance after the treatment with Endotelon or the placebo shows a significant difference:

- 18.0 ± 3.35 cm Hg using Endotelon
- 15.5 ± 1.30 cm Hg using the placebo

This significant difference ($p < 0.01$) clearly affirms the efficiency of Endotelon.

TREATMENT TOLERANCE

Of the total number of patients treated with Endotelon *the clinical tolerance* was good in 21 of the 28 patients.

- In those with arterial hypertension the tensional figures went down moderately in three cases.
- In one case an eruption caused the treatment to be stopped.

- In three cases the sensation of malaise with palpitations and insomnia were observed in the beginning of the treatment. Treatment was stopped between the second and third week.
- There were some gastro problems that were minor and went away in three patients that did not warrant stopping the treatment.

All told in 28 cases the treatment continued normally in 24 patients and in four it was interrupted for side effects.

From a biological perspective no significant modification of the constants was noted.

CONCLUSION

The effects of Endotelon, evaluated principally on capillary resistance are judged very satisfactorily (amelioration in 18 out of 26 cases or a proportion better than two-thirds).

The efficiency of the product was objectively put into evidence by a double blind study.

Taking into account this efficiency together with a very good tolerance Endotelon appears to be a good and interesting element in the therapy of microcirculation with capillary fragility.