

Changes in Immunological Characteristics of White Blood Cells after Administration of Standardized Mistletoe Extract

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Abstract. After administering standardized mistletoe extract, *Viscum album L.* (Iscador[®] injections of 0.1 mg twice and 1.0 mg in defined intervals) the functional characteristics of microcirculation and immunological behavior of the white blood cells in different target tissues (derma, intestine) were investigated in healthy volunteers by vital microscopic investigation over 13 days of observation. The investigations showed a temporarily improved function of the microcirculation and an increased adhesion and transmigration of white blood cells in the target tissue areas. This observation was evaluated as a biologically relevant immunomodulation. Further investigations under pathophysiological conditions with regard to complementary administration of the test substance (e.g. to cancer patients) appear promising.

For decades, standardized mistletoe extract (*Viscum album L.*) has been used as complementary treatment for benign and malignant tumors, for accompanying disturbances of the blood constituting organs, to stimulate bone marrow function, as prophylaxis against neoplastic relapse and to treat precancerous conditions. However, up to now, therapeutical effectiveness has not been adequately investigated or pathophysiologically, immunologically and pharmacologically substantiated. The proof of effectiveness continues to be the object of controversial discussion [1-9]. In a series of reports on experimental and clinical trials, therapeutic success was discussed in connection with immune stimulation, inhibition of the growth of malignant tumors, relief of cancer pain, stimulation of processes regulating body temperature, and improvement of quality of life (10-24).

After subcutaneous injections of standardized mistletoe extract, local reactions appear at the injection site. These individually different skin reactions are interpreted by some authors as undesirable side-effects of mistletoe extract

therapy. Various opinions about their appearance, extent and accompanying reactions are expressed with a view towards the desired effects. Although the local reaction after mistletoe extract administration has repeatedly been investigated, there is still no scientific explanation of the immunological significance of this acute, localized reaction. Comparing this reaction with activities of the immune system in the skin leads to the assumption that the local reaction may be a predictor of drug effectiveness. This, however, must be proven systematically (9,23).

By vital microscopic and reflection spectrometric measurements, the authors investigated the functional characteristics of microcirculation and behavior of white blood cells in the area of the local reaction. Furthermore, whether characteristic changes can be determined in other immunologically active organs was investigated. Increased understanding was expected from the results of these tests with regard to the question as to whether and how a therapeutically relevant immunomodulation can be achieved by mistletoe extract administration.

Materials and Methods

The influence of standardized mistletoe extract on the local microcirculation, on the behavior of white blood cells and on a communication protein of leukocytes in the cutis / subcutis and in intestinal-tract tissue was measured in a randomly defined group of volunteers.

Healthy volunteers (male Caucasians N = 12) with comparable constitutional data (mean values, \pm standard deviations) were recruited:

age, 39.2 years (\pm 3.78);
body weight, 78.1 kg (\pm 2.51)
body height, 174.9 cm (\pm 1.98)

The standardized mistletoe extract *Iscador*[®] QU spezial (WELEDA AG, Schwäbisch Gmünd, Germany) served as the test medication. Dosages were 0.1 mg and 1.0 mg for subcutaneous injection. The injection point was in the Regio abdominalis media, Pars umbilicalis – cranial and near the Pars lateralis sinistra or the Pars lateralis dextra. The localization of the area of administration could be reproduced precisely with the help of a stereotaxis. Defined injections of the test medication were given by an automatic injector (micromanipulator) as for the Tela subcutanea (sterile one-way needles with size 20 cannula

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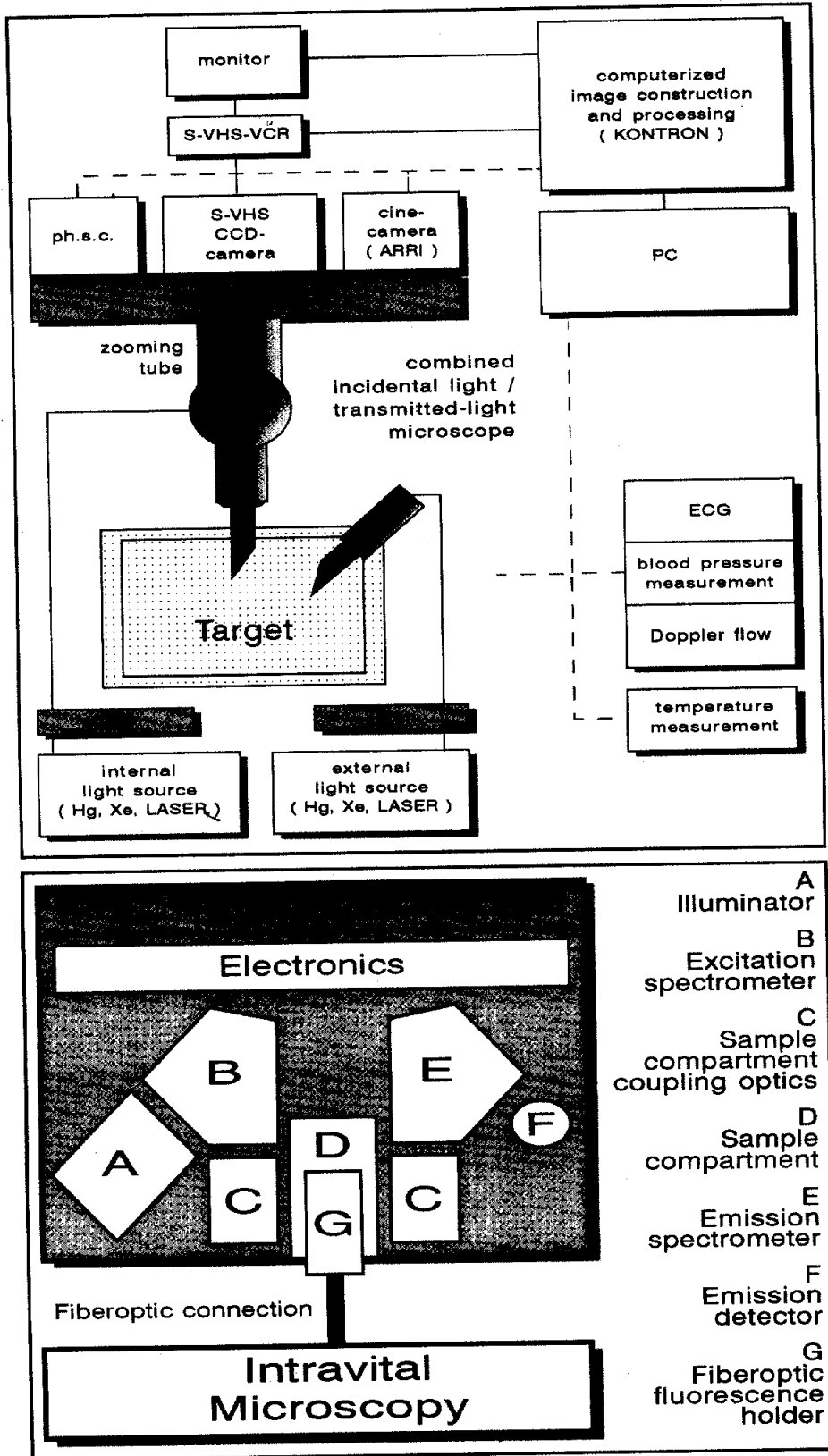
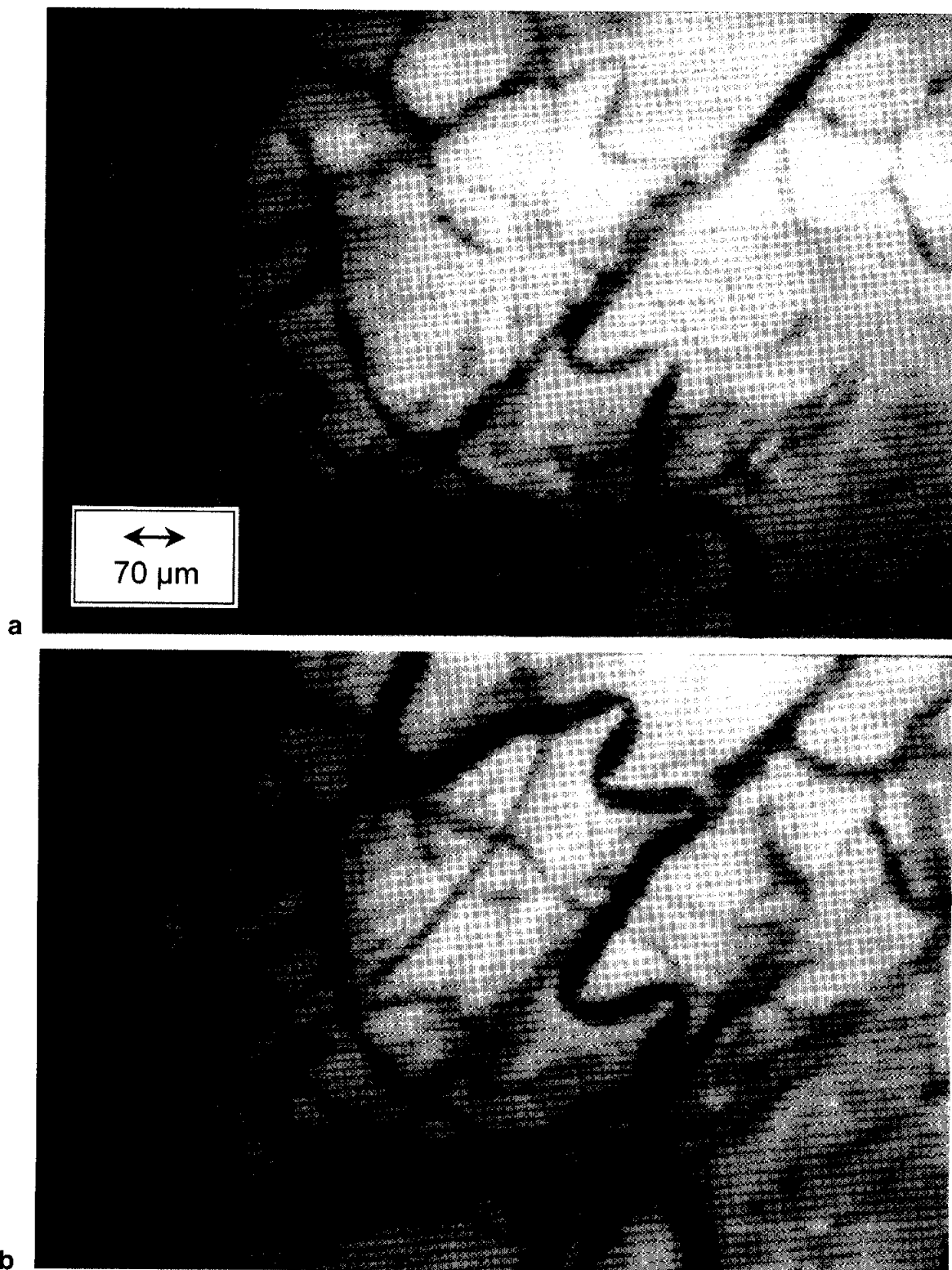


Figure 1. Diagram of the investigation unit.



Figures 2a, 2b. Vital microscopic examples of the functional condition of the microcirculation of a volunteer before and after mistletoe extract injections from the same target region (derma / injection point). mf 1/2000 s; microvascular networks in the cutis / subcutis (arterioles, capillaries, venules). a – microperfusion and distribution condition on day 0 (before the mistletoe extract injection). b – improved microperfusion and distribution condition on day 5 (after the third mistletoe injection).