

Districtual Hydrolipodystrophy

Vincenzo Rialdi

Vevy Europe S.p.A., 18 via Semeria, 16131 Genova, Italy

Districtual Hydrolipodystrophy, commonly known as cellulitis, is caused by a faulty lipidic metabolism involving predisposing genetic factors and lifestyle errors.

This type of dystrophy is supported and worsened by estrogens which favour water retention that tends to be even more marked in sloping areas where the muscle is often less contracted and lipids therefore deposit more easily.

This is associated to a thickening of the adipose lobules which characterize the buttocks and the rear of the thighs since these areas are more often subject to pressure due to continuous sitting posture.

Causes

These include many acquired errors which can hasten hereditary predisposition, i.e: insufficient intake of liquids (especially water which increases local disintoxication); poor dietary habits (it is well known that some substances have a strong irritating action on the liver and affect the veins as well); over exposure to the sun (which causes dilation of the vein wall and thus a decrease in its elasticity and an increase in its permeability, as well as effusion which upsets the whole area), excessive nicotin intake (a well known constrictor of the arterioles).

Iodotrat

As far as cellulitis is concerned, a decrease in both the number of mastocytes and in the granules they contain has been observed since the granules are mainly located near the blood vessels of the connective tissue which becomes asphyxiated due to a vasosclerotic reaction.

When Iodotrat is present the number of mast cells and the presence of granules increase through an action which is likely receptor-mediated. The Iodotrat molecule activates the membrane beta-receptors by interfering with membrane polarity and by opening the calcium channels. This effect cannot be seen with other organic iodated compounds, or with active iodine and its salts (iodides), or with iodated molecules such as thyroxine.

Its Action on Mastocytes

The activation of mastocytes, whose duty is to release vasoactive substances (histamine, heparin, serotonin) which have accumulated as granules in the cytoplasm, is of fundamental importance.

Under normal circumstances the granule moves towards the cell periphery and its membrane blends with the plasmalemma thus causing its contents to be expelled.

Its Action on Lipid Metabolism.

The improved circulation triggers mobilization of lipids in the beta-oxidation circuit.

This resolves a typical cellulitis problem:

$$\begin{array}{c} \text{active liposynthesis} \\ + \\ \text{extremely slow and incomplete catabolism} \\ = \\ \text{adipocyte flooding} \\ \text{numbing of the receptors} \\ \text{reduced synthesis of the lipolytic enzymes} \end{array}$$

whose task is to transform triglycerides
into glycerol and fatty acids

Histologic and Clinical Evaluation

By using Iodotrat, we observed a considerable reduction of inflammatory lymph cell infiltration and a gradual regression of interstitial oedema accordingly with a decrease in size of the treated area (measured in centimeters). This was associated with an improvement of the palpated skin as seen during clinical testing.

The efficacy of cosmetic treatment on cellulitis is still under debate.

Although we are well aware that cosmetic treatment cannot be a substitute for clinical or surgical treatment, it can be truly useful and not simply an issue regarding comfort.

A modern anti-cellulitis formulation may be both beneficial and risk-free, provided that the newly acquired knowledge concerning the biochemical effects on the application site is duly taken into account.

Active principle

The use of elementary iodine is forbidden in cosmetic products. Inorganic iodine (K or Na salts) is highly irritant. Complexed iodine (PVP, cetyl) releases elementary iodine.

Iodotrat is a stable and thermostable, non transferable, organic iodine whose use is allowed in cosmetics. [1]. The optimum dosage of Iodotrat is 0.6 – 0.8%.

Studies have been carried out experimenting various percentages and it has been found that much higher doses do not improve results. This is further supported by the fact that the concentration remains unaltered per time and surface unit due to factors related to increased circulation drainage and to saturation of the enzymatic systems.

The amount of iodine contained in a daily dose (0.8% in emulsion) which actually penetrates the horny layer (about 20%) is sufficient to obtain the desired effect, without reaching blood concentration levels that might alter the physiology of the body. Iodotrat is used by the cell and binds to serum proteins. The amount of iodine contained in a complete application does not exceed the iodine content found in 200 gr. of bananas [2].

Iodotrat is a low molecular weight (293 dalton), stable, organic molecule. It is easily water soluble, purified by crystallization, with no free iodine and remains stable even at temperatures above 80°C. It is also UV lightfast and UV resistant. Furthermore, unlike escine it exerts no hemolytic action, it causes no myolysis as do theophylline, theobromine, caffeine and aminophylline, and it is non-allergenic unlike protease. It is effective at low concentrations (0.6 - 0.8% in emulsion or gel and 6 - 8% in products for iontophoresis and in reducer baths). Its eudermal pH value at application dosages is 5.5. Furthermore it is also a safe active principle, having passed all the tests listed in Table 1.

Table 1

acute oral and i.p. toxicity
subacute toxicity [15 wks]
chronic toxicity [6 months]
eye irritation
acute and subacute skin irritation
Embryotoxicity and teratogenicity
Carcinogenicity
skin sensitization [Magnusson and Kligman]

¹ Zedomine and Zedomine-2, compounds of essential oils, are powerful synergizers of Iodotrat, which are able to activate microcirculation, lymphatic drainage and tissue exchange.

² It is well known that fruit has a thirty times higher iodine content than fish, fifteen times higher than vegetables, ten times higher than meat, seven times higher than cheese and five times higher than bread and cereals.

skin sensitization in man [Quisno]

Formulation

An O/W emulsion was formulated [3] with great care to ensure that the introduction of Iodotrat would not alter its characteristics and that the active principle as such would not be altered. Table 2.

O/W EMULSION 58.3667		
function	ingredient	trade name
Emulsifier	C12-C20 PEG-8 Alkyl Ester	XALIFIN-15
Sebum-like Emollient	C10-C18 Triglyceride	NESATOL
Consistency Factor	Hydrogenated C12-C18 Triglyceride	LIPOCERITE
Microcirc. / Lymphatic drainage enh.	Zedoary, Ginger, Clove EOs	ZEDOMINE-2
Preservative	Parabens in Glycophenylether 99.9%	UNDEBENZOFENE-C
Co-emulsifier / Vehicle Booster	PEG-20 Myristate - PEG-20 Palmitate	XALIDRENE
Humectant	Glycerin	GLICERINA
Water	Water	ACQUA DEM.
Active	TEA-Hydroiodide	IODOTRAT
pH Balancer	Glucamine	DESAMINA
Viscosity Contr. Agent - Humectant	PEG-12 Cellulose	LIPORAMNOSAN
Fragrance Corrector	Perfume	LIPOESSENZIALE - L3

Thermal stability and photosensitivity

Five milliliters of the emulsion were poured into cylindrical, graduated, transparent, vacuum sealed glass vessels. These vessels were then stored under various conditions: in the dark, in direct sunlight, and at temperatures of +5°C, +40°C, +55°C.

Readings were carried out every day without removing the samples. Table F1 shows that our observations after 60 days confirmed the full stability of the product. (Fig. 1)

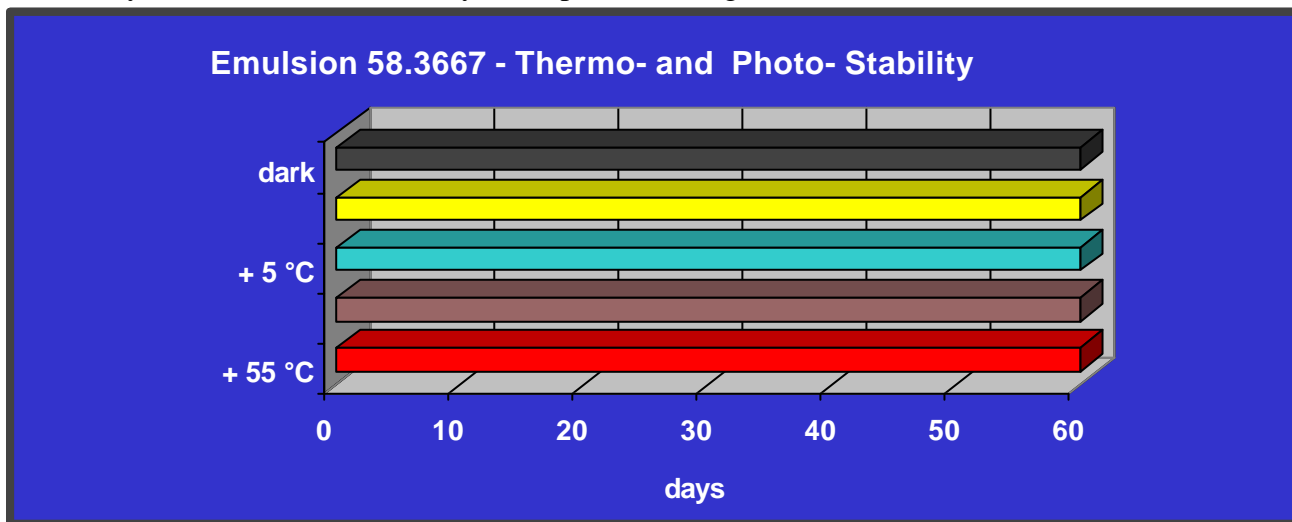
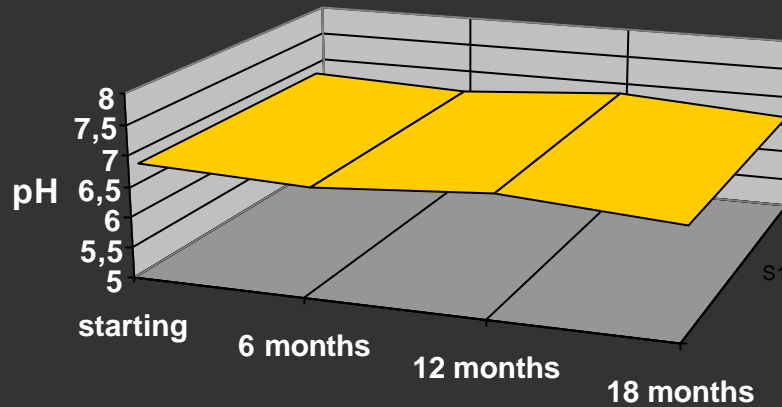


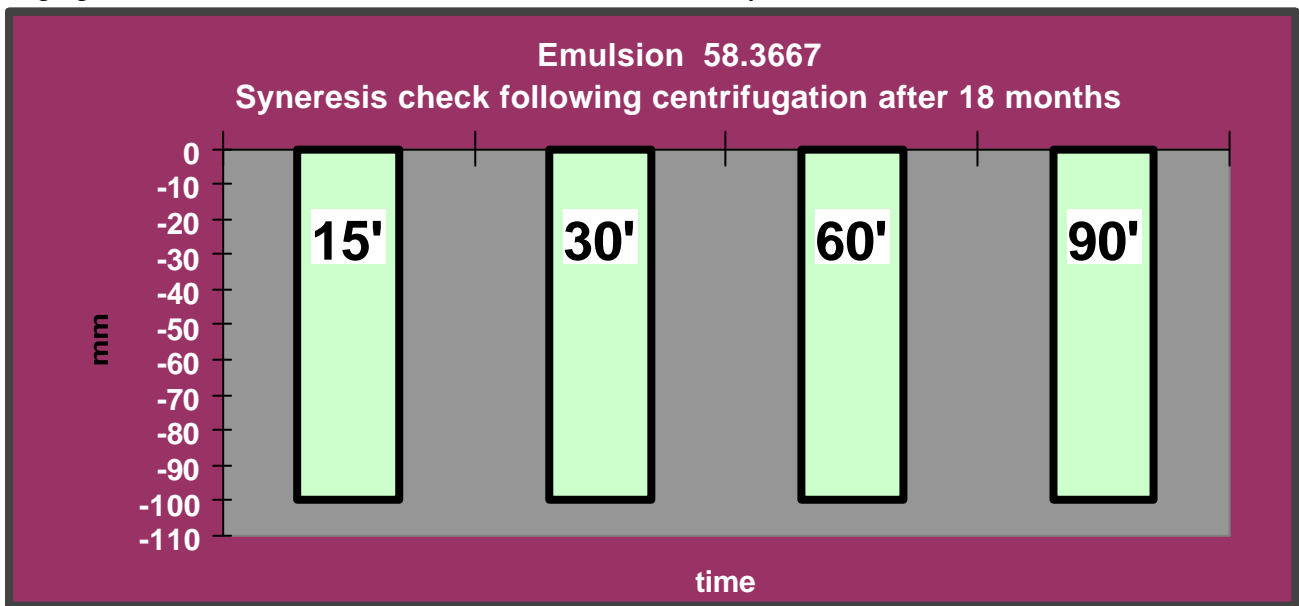
Table F2 shows that pH variations over 18 months are negligible or may only be due to the sensitivity of the measuring instrument.

³ Besides other components described in the relevant technical sheets, it should be pointed out that the main aim of introducing Xalidrene in the aqueous phase is to increase fluidity during its application and to micronize the particles of the lipidic phase so as to speed up the absorption of the active principle rather than simply to heighten its co-emulsifying action.

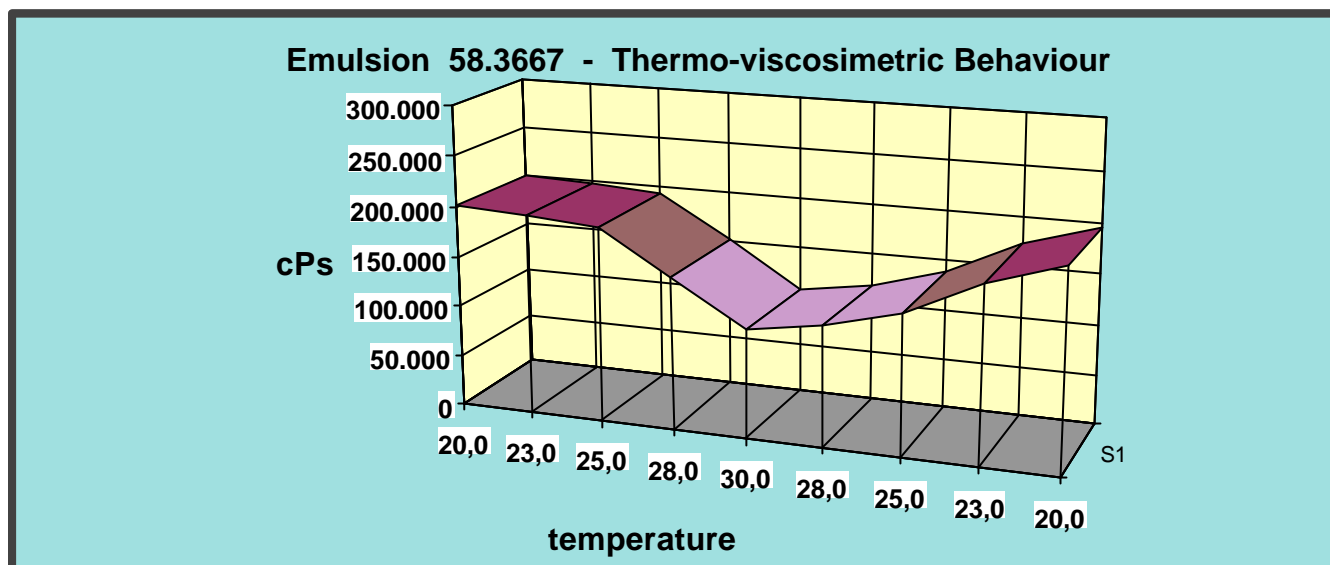
Emulsion 58.3667 - pH variations in 18 months



Syneresis checks were also performed repeatedly over an 18-month period by centrifugation in steps ranging between 15 and 90 minutes. Table F3 shows that no syneresis occurred.



During the same observation period (i.e.18 months), thermo-viscosimetric behaviour was assessed between 20° and 30°C.The results (as shown in Table F4) which are practically superimposable, are once again more than satisfactory.

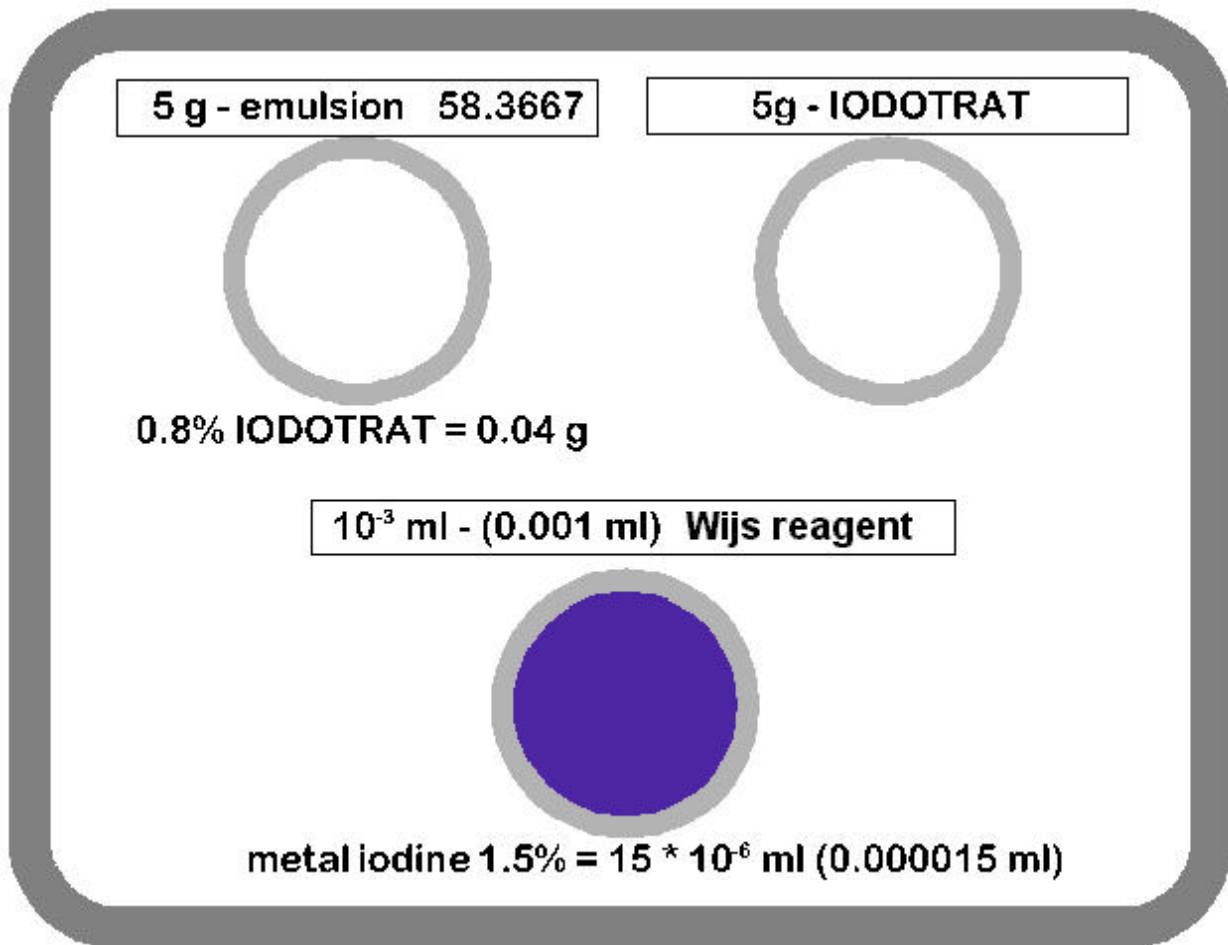


Qualitative determination of free metal iodine.

Five grams of the substance to be tested are poured into a conical flask and solubilized with chloroform and a 1:1 alcohol-ether solution. The presence of metal iodine is confirmed by a characteristic purplish-blue colour when 20 ml of a 10% potassium iodide solution and 1 ml starch are added.

Five g of the previously mentioned emulsion and 5 g of pure Iodotrat, both placed in a boiling water bath for 10 minutes were repeatedly tested over the 18 months following their preparation. Fig. F5 shows the following results: no colouring of the emulsion and Iodotrat sample, while colouring occurred for the Wjis [4] reagent which was used as a test substance.

⁴ Wjis reagent was used to determine the iodine number. The Iodine (I₂) content of the reagent will fix onto the double bonds and determination is thus obtained by retrotitration.



This guarantees that Iodotrat as such, or in emulsion, remains absolutely stable even under difficult conditions and that it can therefore be considered as a resolute, safe and effective active principle.