

## The exaggerated employ of expensive biological actives as ingredients in biomedical remedies are necessary to defeat bedsores.

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**Abstract:** Bedsores are injuries to skin and underlying tissue resulting from prolonged pressure on the skin that occur especially in dependent old patient forced to immobility on bed. Common treatments provide the simple moisturizing of the purulent area thanks to powders that are apt to uptake pus and other organic fluid (as Unna's ointment or vanishing creams, containing Magnesia usta, Kieselguhr, Oenothera oil, Borrage officinalis or Tocopheryl acetate), but they do not approach the chief problem of vascularization that is always decreased.

**Keywords:** bedsores, Unna's ointment, SDTI, vascularization.

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### I. INTRODUCTION

Bedsores — also called pressure ulcers and decubitus ulcers — are injuries to skin and underlying tissue resulting from prolonged pressure on the skin. Bedsores most often develop on skin that covers bony areas of the body, such as the heels, ankles, hips and tailbone.

Common treatments provide the simple moisturizing of the purulent area thanks to powders that are apt to uptake pus and other organic fluid (as Unna's ointment or vanishing creams, containing Magnesia usta, Kieselguhr, Oenothera oil, Borrage officinalis or Tocopheryl acetate), but they do not approach the chief problem of vascularization that is always decreased and obstructed by the constant pressure and the perennial prevention of formation of new wounds, that grow bigger and unsafe day after day, since bacteria Gram+, Gram - and anaerobes develop and become seriously perilous.

People most at risk of bedsores are those with a medical condition that limits their ability to change positions or those who spend most of their time in a bed or chair.

Bedsores can develop quickly. Most sores heal with treatment, but some never heal completely.

Here follow the series of all the steps of symptoms that represent the whole syndrome of bedsores:

Discolored skin (purple or dark red)

Blisters that may be blood-filled

Skin that blanches (turns white) when pressed with the finger

Swelling and/or warmth of the skin

Partial thickness of skin lost

Skin is painful and tender to touch

Beginning of ulcer development

Full-thickness loss of skin, but fascia remains intact

Deeper ulcers

In stage III and IV, some people may not feel pain due to extensive destruction of tissue.

Full-thickness tissue loss along with extension to the muscle, bone, tendon, or joint

Pus production even if the most evident stages are in order of importance (1-2-3-4) and latest complications, where there is no specialist able to determine the gravity of the disease.

a) unusual changes in skin color or texture and swelling of the area

b) Pus-like draining

c) An area of skin that feels cooler or warmer to the touch than other areas

d) compromissions of the 18 Tender points (that might be considered the same of the fibromyalgia).

When these areas are compromised the disease reaches its extreme step and it is quite irreversible.

But the very latest stages are two and are very severe:

The "Unstageable" one is when one can't see the bottom of the sore, so one doesn't know how deep it is. Only a very good specialist can stage it once it's cleaned out.

"Suspected Deep Tissue Injury" (SDTI). This is when the surface of the skin looks like a Stage 1 or 2 sore, but underneath the surface it's a Stage 3 or 4.

Bedsore fall into one of several stages based on their depth, severity and other characteristics, albeit when they fall in the "Unstageable phase" or in SDTI, a complete and safe remission is almost always impossible. The degree of skin and tissue damage ranges from red, unbroken skin to a deep injury involving muscle and bone.

Duty of a good biomedical remedy is to avoid that muscles and bones may be ruined irreremediably and in order to do this, the best way is to act synergically both by continuous wound healing (thanks to elevate dosages of allantoin, that is at 3%, instead of 0,5%, the max dosage employed in generical cosmetics) and high dosages of hesperidin. (more than six times as in common market products).

Anyway, common sites of pressure sores are observable in people who use a wheelchair; pressure sores often occur on skin over the following sites:

Tailbone or buttocks

Shoulder blades and spine

Backs of arms and legs where they rest against the chair For people who are confined to a bed, common sites include the following:

Back or sides of the head Shoulder blades"

Hip, lower back or tailbone

Heels, ankles and skin behind the knees.

Bedsore are caused by pressure against the skin that limits blood flow to the skin. Other factors related to limited mobility can make the skin vulnerable to damage and contribute to the development of pressure sores. When almost the 18 tender points are compromised, even vascularization is always injured: a blood flow severe restraint is noticeable and thus blood provision in all these areas is slowed and/or obstructed at all. Now it is known (1) that Hesperidin has been shown to possess a potential inhibitory effect on vascular formation in endothelial cells. However, the fundamental mechanism for the anti-angiogenic activity of hesperidin is not fully understood. The A.A. had evaluated whether hesperidin has anti-angiogenic effects in mouse embryonic stem cell (mES)-derived endothelial-like cells, and human umbilical vascular endothelial cells (HUVECs), and evaluated their mechanism via the AKT/mammalian target of rapamycin (mTOR) signaling pathway. The endothelial cells were treated with several doses of hesperidin (12.5, 25, 50, and 100  $\mu$ M) for 24 h. Cell viability and vascular formation were analyzed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide and tube formation assay, respectively. Alteration of the AKT/mTOR signaling in vascular formation was analyzed by western blot. In addition, a mouse aortic ring assay was used to determine the effect of hesperidin on vascular formation. There were no differences between the viability of mES-derived endothelial-like cells and HUVECs after hesperidin treatment. However, hesperidin significantly inhibited cell migration and tube formation of HUVECs ( $P < 0.05$ ) and suppressed sprouting of microvessels in the mouse aortic ring assay. Moreover, hesperidin suppressed the expression of AKT and mTOR in HUVECs. Taken together, these findings suggest that hesperidin inhibits vascular formation by blocking the AKT/mTOR signaling pathways.

These findings are fundamental to comprehend how higher dosages of hesperidin (1g/100g applied topically to the bedsore at their ultimate step) may exert an exceptional function on angiogenic dynamics, keeping on account that 100 microlitres of a 1% aqueous hesperidin solution is sufficient to suppress the expression of AKT and mTOR in HUVECs in rats that weigh normally 19g.

Hesperidin, since is very small molecular dimension, trespasses completely the epidermal barrier owing to the Fick's law.

And thus, when 100 g of an emulsion containing 1 g of hesperidin is spread onto the entire body, it is sure that there can be detected 0.014 g of the active in 1 kg of the human body weight, instead of 0.00001 g in kg as in the case of the rat body.

Moreover, it is clear that forced immobility may drive often to gout arthritis with a serious accumulation of sodium urate in extremities.

Women after 75 y. especially, when forced to bed, show too often swollen heels and feet and therapy with allopurinol has been always advised, even in case of purulent bedsore, so that this cure is routine.

Now it is known that there is a specific enzyme (uricase) that is able to encourage the reaction:

$\text{urate} + \text{O}_2 + \text{H}_2\text{O} > \text{allantoin} + \text{H}_2\text{O} + \text{CO}_2$ .

Although, vice versa, when great dosages of allantoin are added in such a reaction, allantoin is able to create more urates and  $\text{O}_2$ .

$\text{O}_2$  is too much important for the vascularization as well and urates can be eliminated easily thanks to low dosages of allopurinol (2).

## **II. MATERIALS AND METHODS**

This is for this reason that we have employed massive dosages of allantoin, so that its use becomes functional and not only aesthetic or cosmetic as well.

The formula of this revisited Unna's ointment is the following:

allantoin  
shea butter  
troxerutin  
borago officinalis seed oil  
hesperidin  
olea europaea fruit oil  
panthenol  
silver citrate  
sodium benzoate  
lactic acid  
potassium sorbate  
hyaluronic acid  
chlorhexidine digluconate  
ceramide 3  
ceramide 6  
ceramide 1.

Besides allantoin and hesperidin, the most important and essential ingredients must be considered:

troxerutin that is a flavonoid derived from rutin and is isolated from *Sophora japonica*, the Japanese pagoda tree and used as a vasoprotective.[3]

shea butter, considered as one of the most humectant agents in cosmeticology.

*Borago officinalis* oil and *olea europaea*, hyaluronic acid that are emollients able to maintain soft and matt skin when injured, and all ceramides are valuable for this type of dermal function.

It is mandatory to stress that:

meanwhile  
sodium benzoate  
lactic acid

potassium sorbate are useful as preservatives and antioxidants for the cosmetic item, panthenol, silver citrate and chlorhexidine digluconate are expressly added in formula to avoid the bacterial outbreak during the purulent phase of the syndrome.

We have prayed 12 nurses working in a private clinic for dependent old patients to use our ointment to treat severe bedsores (from II to all the latest stages) three times pro day for five days.

They were suggested, indeed, to use abundantly the ointment especially on the suspected SDTI on the 18 tender areas (where skin is thinner and nearer to bones).

They used to fill the holes directly with the ointment and let it act all through the night, in the most serious cases.

## **III. III.RESULTS**

After five days all the patients who presented SDTI in more than 7-8 tender spots, showed a renewed skin, well vascularized and did not manifest any sort of pain, warmth or swelling of the skin.

The thickness between the injured skin and the underlying bone was fully restored.

## **IV. CONCLUSIONS**

In order to definitively combat a syndrome that is too often underestimated and so complex that does not permit to focalize the attention on single factors of the same disease, it is important to employ exaggerated dosages of pure biological actives (like hesperidin, allantoin and troxerutin) that are useful to restore vascularization and optimization of the skin property and safeness.

Generally these ingredients, because of their elevate cost are used sparingly and in not adequate dosages.

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