

Preparation for topical use, based on HCG-C® (Complex of two fractions of Curcuma extract dispersed in BioActive functional Hydro-gel)













## VO

parabens, phthalates dimethicone, talc bismuth oxychloride carmine, polysobutene, mineral oil, red 7, red 28, yellow 5 synthetic fragrances GMO's

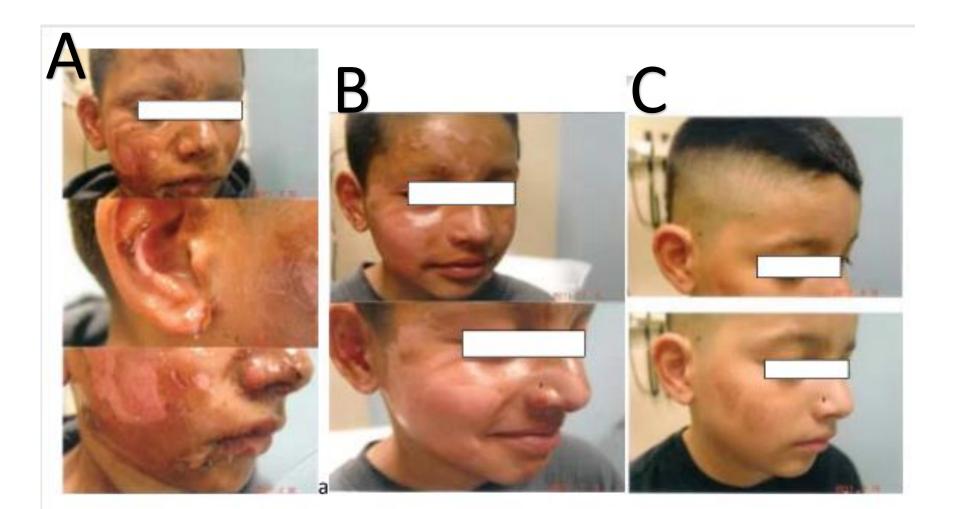
## USEFUL FOR

Post-Sores and operative Erythemes, Radiodermitis infectious **Ulcers** burns scars

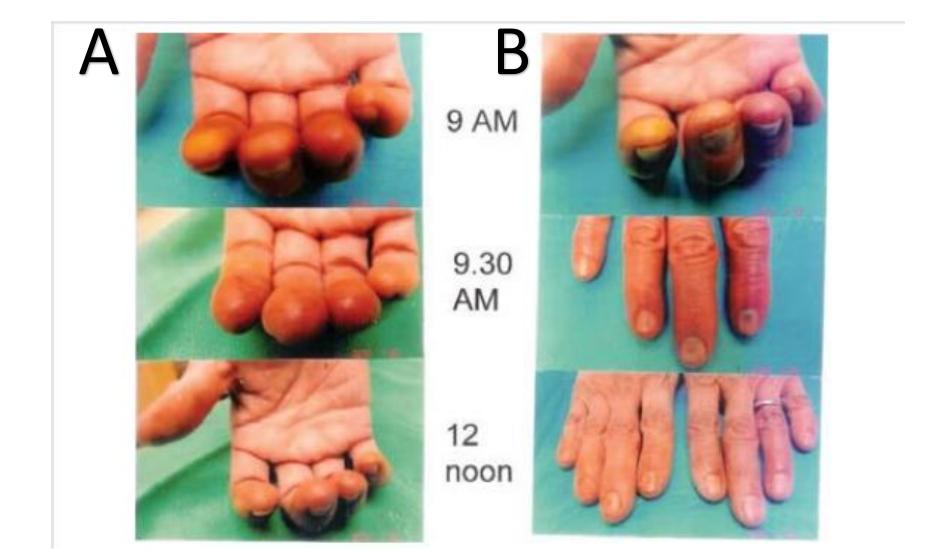


3rd degree burn following radiotherapy treatment for nasopharyngeal carcinoma. The patient was treated with Curcumin in Hydrogel (HGC-C®) for topical use with specific bendage once-administered (about 3ml). Conclusions: almost complete reconstruction of the dermal and epidermal tissue, without purulent exudate and keratosis. The patient during the treatment of Radiotherapy has daily taken Curcumin in Hydrogel (HGC-C®) for oral use (per os) without any oral manifestation of the typical diseases derived from the radio: mucositis, canker sores, candida, etc...

(left-A panels): second degree burns seen 4 days later; (central panels-B): rapid healing 5 days later with frequent application of topical curcumin IN HYDROGEL.; c. (right-C panels): healing without detectable scars with mild post-inflammatory pigmentation 6 weeks later.



(left-A panels) shows the fingers after crushing; of. (panels on the right-B): improvement 3 hours later after frequent applications of high concentration topical curcumin IN HYDROGEL.



(upper panel-A): excision of the right chin for basal cell carcinoma; (central panel-B): residual scars; (lower panel-C): improvement of the scar after the application of topical curcumin IN HYDROGEL concentrated twice a day.



(left-A panels) shows a patient with acne with strong follicular obstruction; (panels on the right-B) show an improvement after application of topical curcumin IN HYDROGEL and vitamin A at high doses



**Diabetic patient** (HBgl 7,5) a.68, hypertensive, affected by polycythemia for 3 years (platelets one million) in therapy with antiplatelet agents and ONCOCARBIDE, Emergence of ulcer f.esterna leg ds at the level of the external malleolus from 1 year, very painful and hypersecretive. Treated with collagenase and gauze grease .. Start HGC-C HYDROGEL both locally and systemically and begins a progressive improvement both locally and from the point of view of pain



Patient (M) years 74, hypertensive, smoker, dyslipidemic, with AOP II STAGES in good compensation (stenosis femoral axis sup dx with ABI 0.8) and MVC IV CLASS. Occurrence of **ulcer malleolar** region internal ankle ds from about 9 months. The ulcer appeared dry, with sharp edges to peak on the bottom, partially fibrinous bottom, red with dry periulcerosa skin, desquamated with the objective signs of MVC AND VARICES TRONCULARS



Patient (M) 58 years old **diabetic** 18 years in good compensation (6.5 glycated), hypertensive, smoker, from 5 months after a trauma an external right leg lesion is formed, .It presents with **leg edema** (3 -4 cm), **ulcer hyper-sensible ulcer**, very painful, edematous and reddened edges, red-violet background, partially covered by a layer of slough. Elastocompressive bandage, cleansing with a sodium hypochlorite solution, iodine cadexomer, hydrofiber for two days.



Patient with **SCLERODERMIA** 77years, severe respiratory insufflation, OXYGENOTHERAPY, IRC, CARDIOPATHICS, ANEMIC (10gr Hb), IPOPROTEINEMIA, ONE YEARS appearance of a foot ulcer ulcer treated with collagenase, medicationsorbents, HGC-C HYDROGEL FOR OS and negative therapy



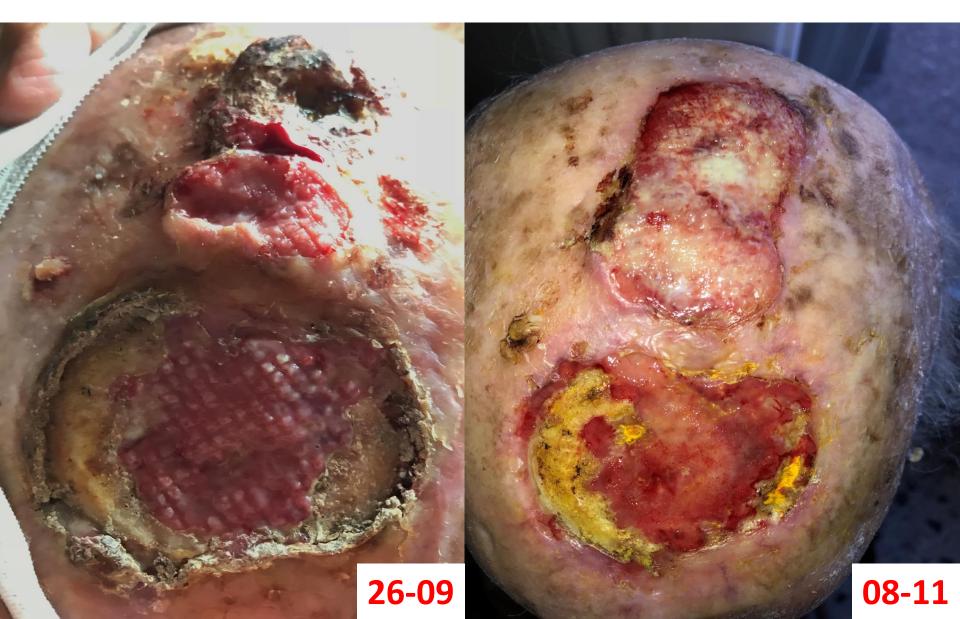
Same patient see again JANUARY 18 with a **new ulcer f.external left leg**, accompanied with increasing pain, hypersecernent, TER: DETERGENT / COLLAGENASIS AND FOAM-HGC-C HYDROGEL FOR OS 1X2



Patient (F) 80 years with **Polycythemia** (700,000 platelets) in therapy with hydroxyurea. From 3 months appearance of ulcer f.est. Leg sn. Detersion - HGC-C IN HYDROGEL per os 1 sachet of E by topical-advanced dressing with hydrophobra plus foam. Medication in alternate days



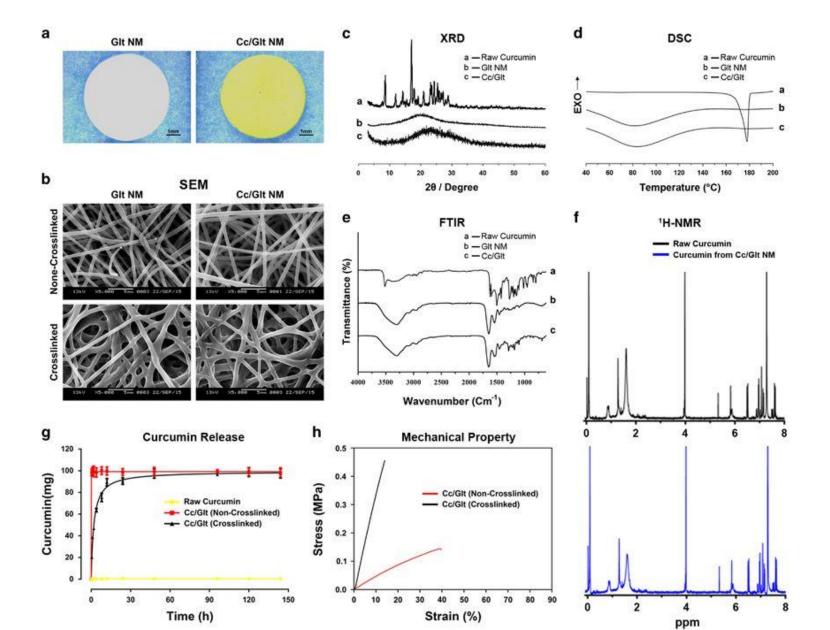
## Patient male, 93, hypertensive, January 18 surgery ch. For epithelioma squamo-cellular frontal region



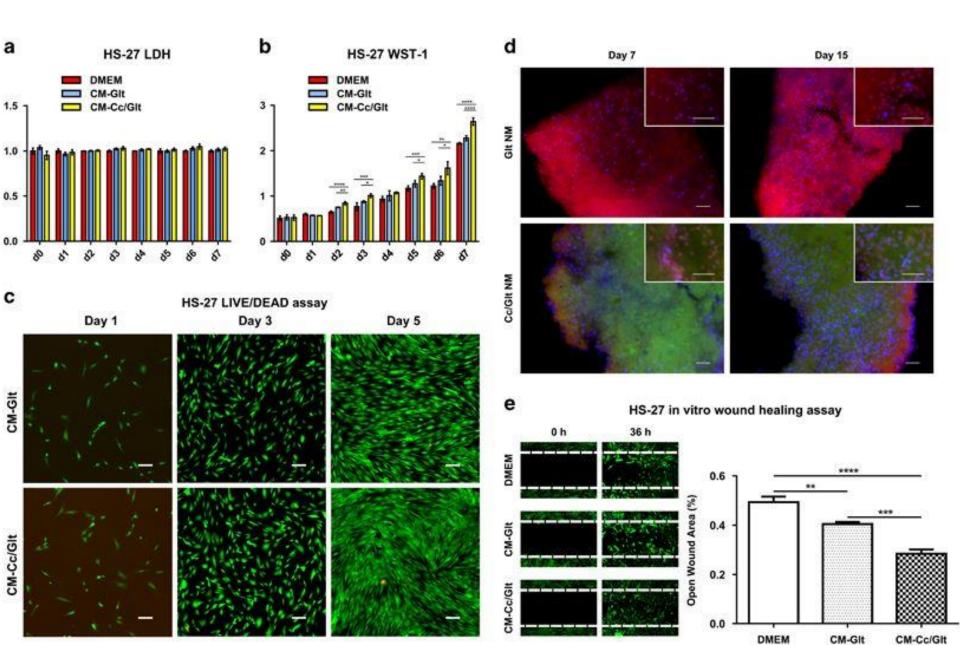
## 1 – The Concept (HGC-C®)

Interaction between curcumin and gelatin (HGC-C HYDROGEL), most likely due to the formation of an amorphous solid dispersion, a known condition for increasing drug dissolution. On the other hand, the hydrogen bonding between curcumin and gelatin, would inhibit curcumin crystallization and let the compound precipitate out in the amorphous form, resulting in increased curcumin solubility. Hence, it is likely to be that gelatin inhibited the association of curcumin molecules to form crystal nuclei and subsequent crystal growth in the nanofibers during the electrospinning process. Most importantly, however, the chemical structure of curcumin was preserved throughout the entire process, which is of crucial importance to exert its biological effects after being released.

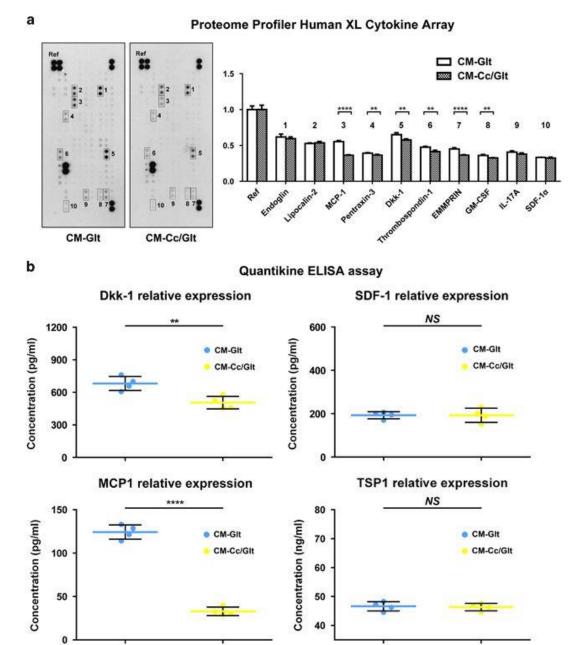
## Nano-formulated curcumin accelerates acute wound healing through Dkk-1-mediated fibroblast mobilization and MCP-1-mediated anti-inflammation



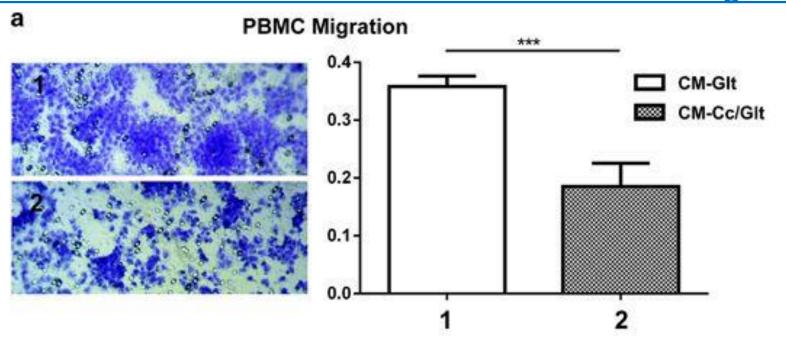
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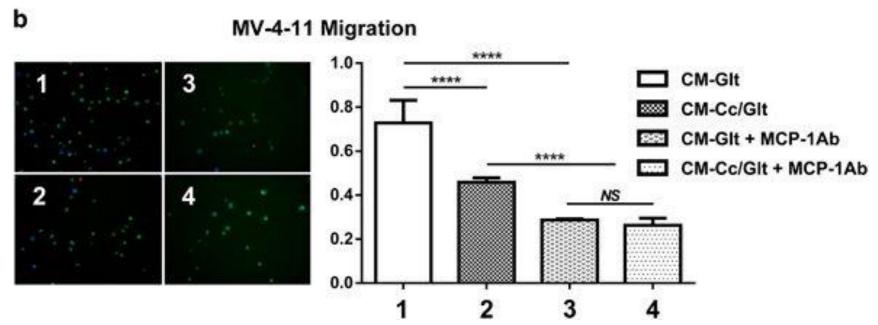


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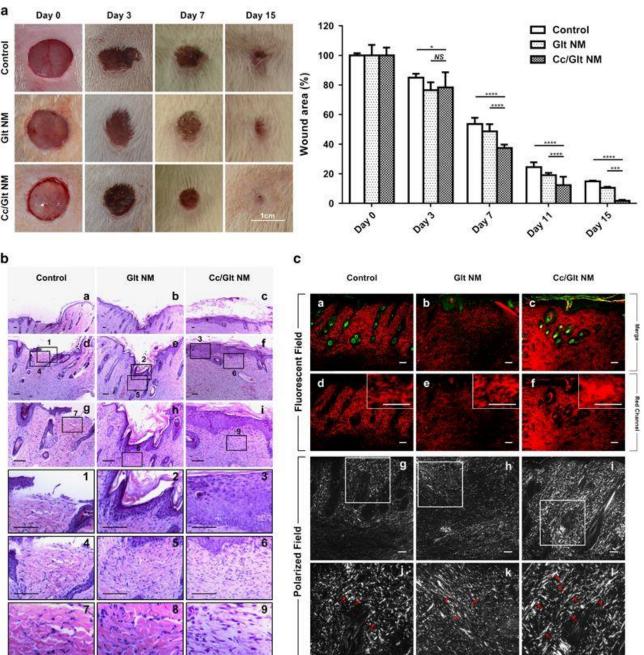


#### Curcumin-induced anti-inflammation is mediated through MCP-1



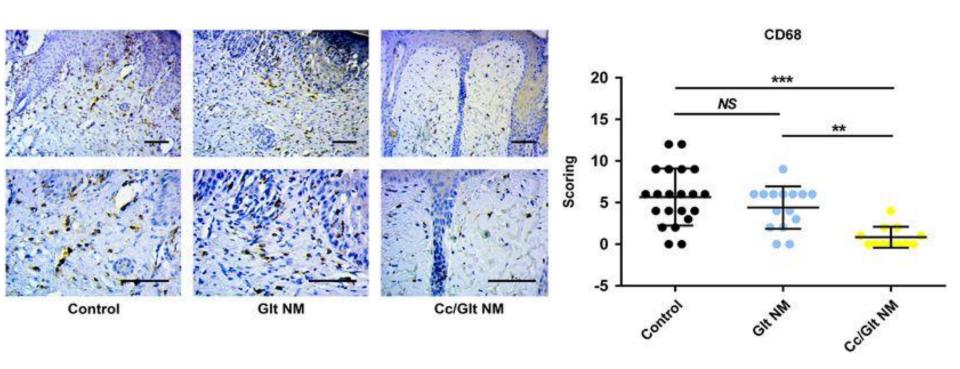


#### **Wound healing** in vivo



- (a) Cc/Glt NM accelerates wound closure.
- (**b**) Cc/Glt NM enhances dermal regeneration
- (c) Cc/Glt NM enhances collagen deposition.

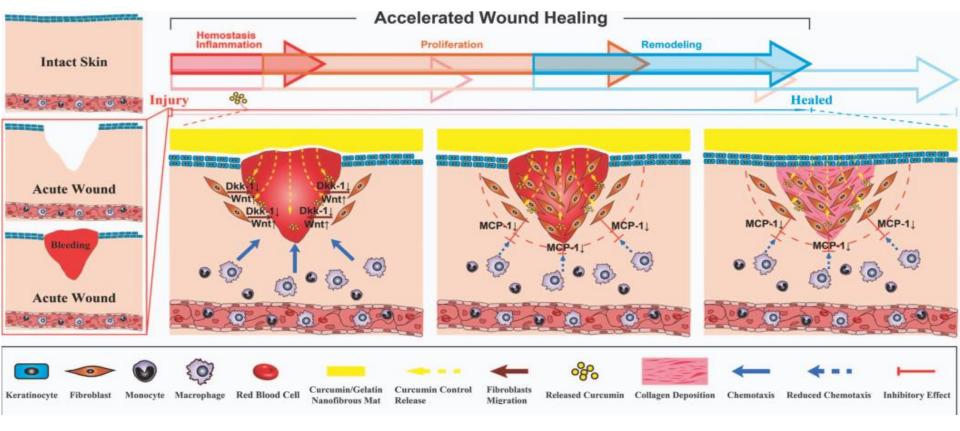
### Topical application of Nanoformulated Curcumin in Hydrogel inhibits macrophage infiltration in vivo.



# 2 – Molecular pathway (HGC-C®)

Delivered curcumin was shown to recruit wound site fibroblasts in vitro and in vivo by inducing proliferation and migration, which is at least partially mediated by Dkk-1. Our results agree with those of a previous report showing decreased expression of Dkk-1 and enhanced expression of β-catenin in fibroblasts from pachydermoperiostosis (abnormal fibroblast proliferation) patients. Similarly, the Dkk-1-mediated Wnt signaling pathway has also been found as a positive regulator of cell migration in other tissue such as breast cancer.

Given that the Wnt signaling cascade with its antagonist Dkk-1 has been proposed to have crucial roles for maintaining homeostasis of a variety of tissues including the skin, and that the physiologic Dkk-1 level is of vital importance to maintaining its biological functions, we speculate that curcumin could precisely control the Dkk-1 level in a temporospatial manner to regulate the downstream Wnt signaling pathway, as Dkk-1 has been shown to participate in a negative feedback loop in Wnt signaling as well. However, more studies are required to fully elucidate its less well-understood role in wound healing.



#### Diagram of the potential mechanism for accelerated wound healing induced by

**curcumin.** Following an injury, topically applied HGC-C leads to the controlled release of bioactive curcumin, which in turn mobilizes wound site fibrils through increased cell proliferation and migration, a process partially mediated by the Wnt /  $\beta$  pathway -catenin regulated by Dkk-1 signaling. Meanwhile, fibroblasts decrease the expression of MCP-1, which mediates the monocyte / macrophage chemotaxis, leading to a lasting inhibition of the inflammatory response during the healing process. As a result, the wound environment is more favorable for subsequent healing stages of wounds with faster reepithelialization, granulation tissue formation, collagen deposition and maturation by proliferative fibroblasts.

### 3 - Clinical Application (HGC-C®)

The **first step** is based on the patient's holistic view, so as to arrive at a diagnosis of the possible diseases that the patient suffers that may be the basis of onset of ulcer.

The **second step** is the etiological diagnosis of the ulcer in order to highlight the various characteristics of the ulcer (shape, size, depth, margins, etc.).

Then we move on to the local approach of the ulcer based on the concept of wound bed preparation (preparation of the ulcer bed) that can be summarized by the acronym **TIME.** 

Locally the ulcer is treated, after eliminating any non-viable tissues and having controlled the bacterial load:

- 1) DETERGENT WITH ANTISEPTIC SOLUTION
- 2) APPLICATION OF CURCUDERM ON THE BACKGROUND OF THE ULCERA IN A WAY AS TO RECOVER IT ALL
- 3) CLOSE THE EVERYTHING WITH GREASE OR HYDROPHIBER BENDAGE
- 4) THEN COVER WITH STERIL BENDAGE

AND MEDICATE FROM TWO TO THREE TIMES THE WEEK (OR EVEN ONCE THE WEEK).

IN EVERY CASE THE INTERVAL BETWEEN A MEDICATION AND THE OTHER MAY BE EVALUATED CASE BY CASE ON THE BASIS OF THE ULCER.

