Onion Extract

Julian Poetschke and Gerd G. Gauglitz

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Background

Multiple studies on hypertrophic scar and keloid formation have led to a multitude of therapeutic strategies in order to prevent or attenuate keloid and hypertrophic scar formation. Until today preventing pathologic scarring remains undoubtedly more effective than treating it later on. Thus, avoiding all unnecessary wounds in any patient, whether keloid/hypertrophic scar-prone or not, remains an obvious but imperfect solution. Since delayed epithelialization beyond 10 to 14 days increases the incidence of hypertrophic scarring dramatically [1], achieving rapid epithelialization is mandatory for avoiding excessive scar formation. Particularly, wounds subjected to tension due to motion, body location, or loss of tissue are at increased risk of scar hypertrophy and spreading [2]. Thus, in case of any cutaneous injury, the goal for rapid primary closure of wounds under little to no tension cannot be overstated. In addition to gentle surgical techniques and suitable suture material, careful hemostasis, and intraoperative tissue treatment, the prevention of wound infections and delayed wound healing are extremely important for good scar healing. The incision should be made along the “Langer” lines of the skin and take esthetic subunits (especially in the face) into account. The patient himself or herself should expose fresh scars to little traction, pressure, and stretching, consistently protect them from the sun, and return early to the treating physician as growth increases. If there is a known tendency to formation of keloids and hypertrophic scars, early intralesional injection of triamcinolone acetonide into the fresh surgical wound after surgery may be considered. According to various studies, next to pressure garments, early and regular application of silicone-based products seems to lead to an improvement in scar quality and an accelerated reduction in redness. Current guidelines emphasize the importance of silicone gels and patches for preventive treatment (at the earliest from the 14th postoperative day for at least 2 months) to avoid excessive scars in high-risk patients.

Topical gels containing onion (*Extractum cepae*) extract have been available for more than 60 years treating, preventing, and reducing dermatologic scars and keloids [3]. *Extractum cepae* is reported to have anti-inflammatory, antimicrobial, antiproliferative, and regenerative activities [4]. Several clinical trials have indicated that *Extractum cepae* may prevent pathologic scarring and improves preexisting scars. It has been introduced as a preventional approach for unpleasant hypertrophic scars in current German scar guidelines in 2012 and in current international scar guidelines in 2014.

24.1 Onion Extract

Extractum cepae acts in an anti-inflammatory manner and is bactericidal. It is currently believed that the flavonoids (quercetin and kaempferol) in onion extract play the main role in reducing scar formation through inhibition of fibroblast proliferation and collagen production. A study by Phan and others suggested that these inhibitory effects may be mediated through inhibition of transforming growth factor- β (TGF- β 1, -2) and SMAD proteins by quercetin [5, 6]. Specifically, the authors demonstrated that basal expression and activation of several key proteins in the IGF (insulin-like growth factor)-1 signal pathways were significantly reduced when keloid fibroblast cells were exposed to quercetin. The authors also analyzed keloid fibroblast cells treated with quercetin by means of immunoblotting and electron microscopic approaches. Fibronectin expression was suppressed by quercetin suggesting a strong inhibitory effect of this compound on production of fibronectin. Transmission electron microscopy was performed on keloid fibroblasts with and without quercetin. Keloid fibroblasts without quercetin showed markedly higher density of ECM fibers in a homogeneous ECM, but no ECM deposition was seen in the fibroblasts treated with quercetin, indicating a strong effect of quercetin in the suppression of ECM production and deposition by keloid fibroblasts. In a follow-up study, Phan et al. treated keloid fibroblast cells with quercetin at different concentrations, and cells were then harvested and subjected to immunoblotting analysis. In the pathogenesis of keloids, both IGF-1 and transforming growth factor- β (TGF- β) signaling systems are usually overactive, stimulating fibroblast overproliferation and production of collagen and ECM. The data of Phan and colleagues suggested that quercetin could potentially have an anti-scarring effect by inhibiting the signaling pathway of IGF-1 and TGF- β systems.

It has been further demonstrated that several flavonoids inhibit the antigen-induced histamine release from human basophils, which may be of certain importance since there is evidence to the effect that histamine may accelerate collagen formation.

Today, an increasing body of literature and clinical experience are available testing the ultimate clinical benefit of onion extract-containing scar creams as monotherapy (■ Fig. 24.1) or in combination with other measures (■ Fig. 24.2). Study data on the efficacy of *Extractum cepae* for prevention and treatment of hypertrophic scars or keloids, however, remains inconsistent, and the quality of the studies is relatively poor.

■ **Fig. 24.1** Upper half of the scar has been treated twice daily for 3 months with onion extract gel

Currently several onion extract-containing scar gel preparations do exist that are mainly based on combinations with either allantoin alone or allantoin and heparin.

Willital et al. evaluated the efficacy of *Extractum cepae* in combination with allantoin and heparin on early scars in an uncontrolled, multicenter, prospective observational study in 1268 subjects. In this study, the scar gel was used at least twice daily. The observational period was 4 to 5 months [7]. Data was recorded at start of treatment, after 2–3 months, and after 4–5 months. Even though the authors were able to show some benefit of regular application of an onion extract-containing gel and a considerably high patient satisfaction, the study was completely uncontrolled; did not use any consistent, recognized scar scale; and was thus highly susceptible to bias. For prevention of hypertrophic scars and keloids, a prospective, randomized, controlled non-blinded study on children with surgery on the thorax after 6-month use of a scar gel containing onion extract, allantoin, and heparin observed a less frequent development of excessive scars than in the untreated comparison group [8]. The therapy in the comparative group, however, remained largely unclear with the statement “normal wound therapy.” This is of particular significance, as in a further comparative study on improving scar quality (erythema, pruritus, burning, pain, hypertrophy) between scar gels containing onion extract and a topical agent based on petrolatum, a specific effect of the ingredients could not be proven [9]. It must be considered, however, that the patient number in this study was low, the operations were not performed on specific predilection sites such as the thorax, and thus statistically significant results could have been expected only with very high patient numbers. For treatment of hypertrophic

■ **Fig. 24.2** Before (a) and after (b) three sessions of fractional CO₂ every 4 weeks, in between onion extract-containing scar gel twice daily

scars and keloids, the benefit of a combination of intralesional triamcinolone and an onion extract combinational gel was reported as positive, with both monotherapy with triamcinolone alone and the combination with an additional topical agent containing onion skin extract resulting in statistically significant improvement. A calculation of statistical significance with respect to the differences of the therapy concepts was, nonetheless, not performed in the study [10].

In a prospective randomized controlled trial conducted in China, the use of onion extract was investigated in the prevention of scarring after laser removal of tattoos [11]. Local experience according to the authors found that nearly 25% of Chinese subjects with dark skin (Fitzpatrick types III–IV) developed scarring after laser removal of tattoos. A total of 120 subjects with 144 professional blue-black tattoos were randomized into the onion extract group or the control group. Subjects in the onion extract group applied onion extract to the treatment areas after reepithelialization twice daily in between laser treatment sessions, and subjects in the control group did not apply anything. A total of 52 subjects with 61 tattoos completed the study in the onion extract group. Seven tattoos (11.5%) in seven subjects developed scarring, four subjects (7.7%) had permanent hypopigmentation, and three (5.8%) had permanent hyperpigmentation. The control group comprised 55 subjects with 68 tattoos. Sixteen tattoos (23.5%) in 14 subjects developed scarring, 4 subjects (7.2%) had permanent hypopigmentation, and 5 (9%) had transient hyperpigmentation. According to this publication, the rate of scarring was statistically significantly lower in the onion extract group than in the control group.

It is currently recommended to apply the gel several times daily (usually two to three times a day) with mild massage of the scar tissue. In firm, mature scars use under occlusion or in combination with ultrasound may also be considered. In prophylactic postoperative use, treatment may be started shortly after removal of sutures. In the treatment of open wounds, scar prophylaxis using an onion extract gel should be delayed until complete epithelialization of the wound. Treatment usually continues over several weeks to months. While side effects are generally very low, treatment containing onion extract might be slightly irritating in facial areas, particularly in younger children.

Recently, an onion extract- and allantoin-containing patch has been introduced to the market. This product features an occlusive active release liner with an adhesive layer separated by a micro-air cushion seal.

The so-called overnight intensive patch may be cut to size for small scars or placed side-by-side for larger scars. Its efficacy has been elucidated in an intraindividual randomized, observer-blind, controlled study in adults with post-dermatologic surgery scars [12]. Two scars per subject were randomized to no treatment or overnight treatment with the OIP for 12 to 24 weeks. Scar quality was assessed in a total of 125 subjects using the Patient and Observer Scar Assessment Scale (POSAS) and Global Aesthetic Improvement Scale. The authors found a decrease in observer-assessed POSAS from baseline, which was significantly greater for treated than untreated scars at week 6 and 24. The decrease in patient-assessed POSAS was further significantly greater for the treated scar than the untreated scar at week 12 and 24. Subject- and investigator-evaluated Global Aesthetic Improvement Scale scores were higher for the treated than the untreated scar at all visits. According to the manuscript, all subjects considered the global comfort of the OIP to be good or very good, and no safety concerns were identified. Also, no further studies have been published, testing this rather novel product, and current communications do confirm a high patient satisfaction due to the patient orientation application and a certain benefit for early scarring.

24.2 Conclusion

Scarring following surgery or trauma is difficult to predict, and both physicians and their patients are highly concerned with minimizing scar appearance and value even small improvements in scarring as clinically meaningful. Till to date, preventing pathologic scarring remains undoubtedly more effective than treating it. Next to specific surgical techniques and appropriate general aftercare of fresh wounds, a multitude of scar gels, creams, patches, and ointments are available and are being promoted for scarless wound healing. Next to silicone-based products, onion extract or cepalin has been highlighted as one potential anti-scarring agent over recent years. Although its underlying study data remains in part contradicting regarding its efficacy, onion extract-containing scar creams appear to positively influence scar texture, height, and associated symptoms compared to placebo or untreated control. Based on the recently published German guidelines on scarring, onion extract-containing scar creams may be considered as additional therapy for active hypertrophic scars and for postsurgical prophylaxis of excessive scarring.

Take-Home Messages

- Preventing pathologic scarring remains undoubtedly more effective than treating it.
- Next to silicone-based products, onion extract-containing creams have been shown to positively influence scar maturation if used shortly after wound healing.
- Data remains contradicting, but guidelines have incorporated onion extract in their recommendations on preventing unpleasant scarring.
- Onion extract-containing products are available as creams, ointments, gels, or patches.
- Therapy can be started after complete epithelialization of the wound and should continue for 12 to 24 weeks.
- Onion extract-containing products are safe, and side effects beyond irritation of the treated skin are extremely rare.

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