An investigation to assess adhesion time, tolerability and usability of plain patches for sensitive ulcerative, erosive and erythematous oral lichen planus lesions

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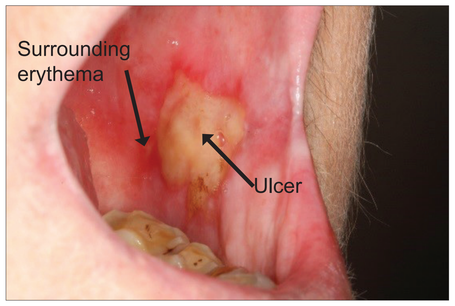
Introduction

Lichen planus is a chronic inflammatory disorder, which can affect skin, nails, hair follicles and mucous membranes. If the oral cavity is affected, oral lichen planus (OLP) patients often suffer from symptomatic lesions experienced as local burning sensations, soreness and pain. Picture illustrates an ulcerative OLP lesion.



The pathomechanism is not fully understood. There is evidence supporting OLP to result from an autoimmune reaction against basal keratinocytes. The finding of infiltrates containing CD8+-T-cells in OLP lesions supports this theory [1]. MHC molecules present antigens to CD8+-T-cells, which then destroy keratinocytes.
The lack of understanding of the exact pathogenetic mechanism limits the therapeutic options to resolution of relapses but a cure of OLP remains to be found., The treatment focus is set on anti-inflammatory agents. First-line therapy for OLP is the topical application of corticosteroids of high or medium potency [2, 3, 4].Systemic therapy is reserved for more severe cases due to the potential side effects. Most topical formulations on the market are designed and approved for such application to the skin. These formulations are not designed for application on moist surfaces as the oral mucosa.

A novel plain patch, the Rivelin® patch, has been developed which can attach to moist surfaces and remain there despite movement. Our aim was to investigate the adhesion time of the Rivelin® plain patch when applied to sensitive ulcerative/erosive and/or atrophic/erythematous OLP lesions. Our secondary objective was the investigation of tolerability, safety and feasibility of Rivelin® patches in the oral cavity of patients with OLP lesions. Exploratory objectives included the investigation of disease activity over time and the effect on pain and functional limitation.

Hypothesis

We tested the hypothesis that Rivelin® patches could be a useful technology for the effective application of interventional drugs to the oral cavity.
Furthermore, the use of Rivelin® patches should be safe and with good tolerability.

Methods

The Rivelin® patch used for this study is an electrospun bilayered patch consisting of a protective layer and a drug-delivery layer, which faces the mucosa [5]. The size of the patch is ~1.3 x 2.5 cm. The protective layer is hydrophobic whereas the drug-delivery layer is hydrophilic. This ensures that the patch remains where it is placed. The patch is flexible and can be attached to any part of the oral cavity including gingiva, tongue or buccal mucosa (Figure 1)

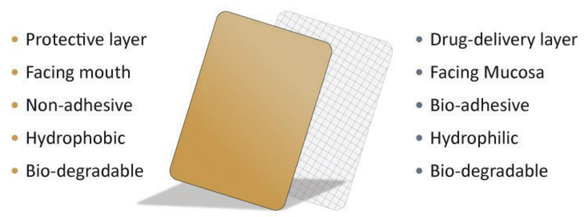


Figure 1. Illustration of the patch layers

The patch consists of bio-degradable material and is, therefore, safe to use, as it will dissolve in the mouth or stomach. The plain patch does not contain any active pharmaceutical component.

We included adult subjects with active OLP seeking treatment for at least one sensitive lesion on gingiva, tongue or buccal mucosa. The lesion treated had to be of a size to be covered by 1-2 patches. All eligible subjects received treatment with the plain patch on one target lesion on gingiva, tongue or buccal mucosa. The treatment period was four weeks with weekly visits to the clinic. Subjects were instructed to place patches two times daily, directly on OLP lesions as instructed at enrollment. At the weekly clinic visit, patch adhesion time, tolerability and usability of the plain patches was assessed. An end of investigation visit 6 was to be performed on Day 29. The status of affected areas as well as the global impression was scored and recorded at baseline by the investigator using the Guy's score [6]. The subjective symptoms were recorded using the Chronic Oral Mucosal Diseases Questionnaire (COMDQ) [7].

The subjects self-administered the plain patch for the entire investigation period Continuous and categorical data was summarized using descriptive statistics and frequency tables. The proportion of successful subjects (≥80% positive applications) was estimated and 95% confidence intervals were constructed using the Wilson score method. Wilson score method was used for the proportion of positive outcomes on each question of the patch sensation questionnaire and the subject-reported feasibility scores.

The study was conducted under GCP and approved by the German authorities, BfArm and local ethical committee.

Results

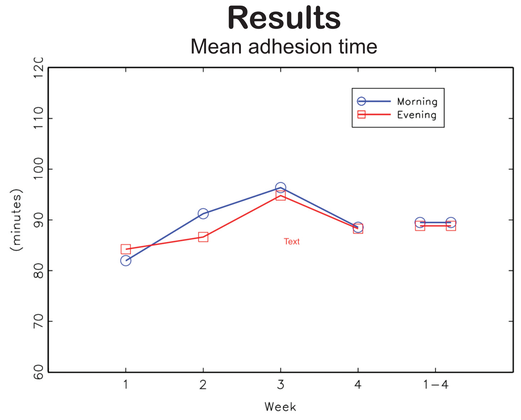


Figure 2. Mean value curves of average adhesion time by study period

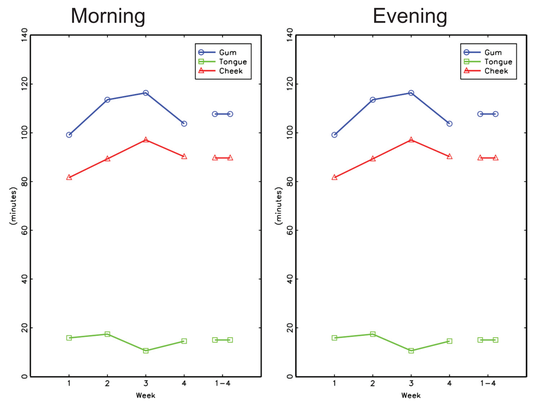


Figure 3. Mean value curves of average adhesion time by study period and target site

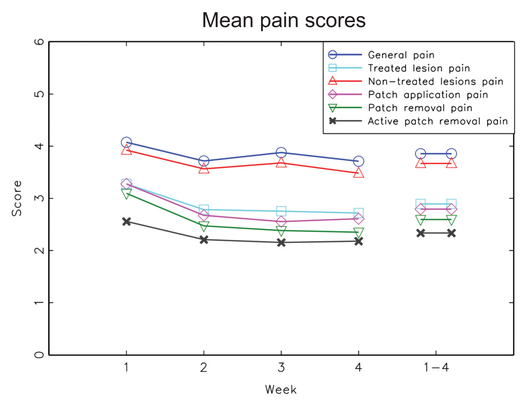


Figure 5. Mean value curves of average pain scores by study period

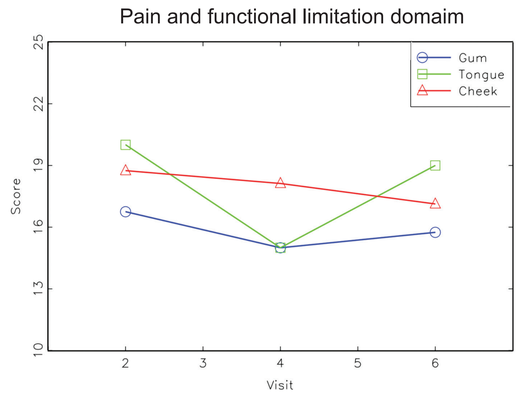


Figure 11. Mean value curves for COMDQ, pain and functional limitation domain by target site, absolute values

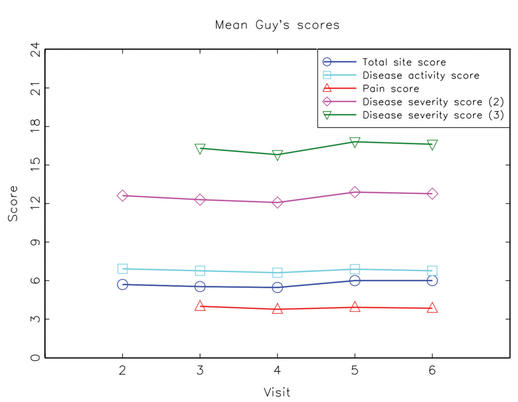


Figure 14. Mean value curves by parameter for Guy's scores, absolute values

Results Summary

13 patients with OLP were enrolled into the study. 9 women and 4 men at a mean age of 63.9 ± 10.8 years were involved. The most common site for the target lesion was the cheek, it was chosen in eight subjects. Four subjects had a target lesion at the gum and only one on the tongue.

Adhesion (mean time) was 90 minutes for morning and 89 minutes for evening applications. Figure 2 shows the mean adhesion time throughout the study, figure 3 displays the adhesion time for the individual regions. If a patch had not detached prior to 120 minutes after application, the patch was supposed to be removed actively (by swirling water or eating) by the subject.

Pain was questioned as general pain, most intensive pain related to the treated lesion and to the untreated lesions, and pain related in connection with application and removal of the patches in the evening. As seen from figure 5, pain scores were stable over the study period.

COMDQ was used to assess the QoL of the patients, mainly focusing on pain and functional limitation. Figure 11 seems to suggest that the subjects remained unchanged.

Guy's score was almost unchanged throughout the study as can be seen in figure 14. The graph only indicates subtle changes.

We were able to demonstrate that the patches adhere well to OLP lesions.

According to the patch sensation questionnaire, the subjects did not find the patches irritating and the application did not provide any challenge to them. The removal was also experienced as easy. As expected, the plain patches did not improve pain or Guy's Score levels. The improvement of subjective and objective symptoms will be addressed in further placebo controlled interventional studies, which will use Rivelin patches with different strengths of Clobetasol propionate and the Rivelin plain patch as placebo.

It also promises to be a safe option. The bilayer technology of the patch ensures a uni directional drug-delivery, whereby spread of medical substances to healthy mucosa will be prevented.

Conclusion

We could demonstrate that Rivelin® patches adhere to OLP lesions and are easy to handle for patients providing a more precise and patient-compliant option for the application of topical treatment to the oral mucosa.

References

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