

CONTACT POINT

Contact allergy to tribenoside: A Rare allergen

Laura Malinauskienė^{1,2}  | Kęstutis Černiauskas^{1,2} | Linas Griguola^{1,2} | Anželika Chomičiene^{1,2}

¹Clinic of Chest Diseases, Institute of Clinical Medicine, Immunology and Allergology, Vilnius University Medical faculty, Vilnius, Lithuania

²Center of Pulmonology and Allergology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

Correspondence

Laura Malinauskienė, Center of Pulmonology and Allergology, Vilnius University Hospital Santaros Klinikos, Santariškių Street 2, Vilnius LT-08661, Lithuania.

Email: laura.malinauskiene@santa.lt

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CASE REPORT

A 48-year-old female patient presented to our clinic with a 2-week history of erythematous and itchy dermatitis around her anus (Figure 1). She had applied Procto-Glyvenol crème (Recordati Industria Chimica e Farmaceutica S.p.A., Milan, Italy), containing tribenoside and lidocaine, for several days to treat haemorrhoids. She suspected that this drug could be responsible for her symptoms and intentionally applied it to her forearm. The next day dermatitis developed, which spread and remained active for 2 weeks.

Patch tests were performed with the European baseline series complemented with lidocaine 5.0% pet., cetyl alcohol 5.0% pet., benzisothiazolinone 0.1% pet. (all from Chemotechnique Diagnostics, Vellinge, Sweden) and Procto-Glyvenol crème “as is”. The results were assessed after day (D)2, D3 and D7 according to ICDRG guidelines (Table 1).



FIGURE 1 Positive patch tests reactions to Procto-Glyvenol crème

As the patient was positive to Procto-Glyvenol crème (Figure 1), further patch testing was carried out with benzoic acid 5.0% pet. (Chemotechnique) and serial dilutions of tribenoside (European

TABLE 1 Positive reactions to tested substances

Tested substance	Reaction on D2/3	Reaction on D7
Nickel sulfate 5.0% pet.	1+	1+
Colophonium 20.0% pet.	2+	2+
Myroxylon pereirae 25.0% pet.	3+	2+
Fragrance mix I 8.0% pet.	3+	3+
Propolis 10.0% pet.	3+	3+
Budesonide 0.01% pet.	2+	3+
Procto-Glyvenol creme	3+	3+
Textile dye mix 7.0% pet.	1+	1+
Disperse Orange 3 1.0% pet.	1+	Negative
Methyldibromo glutaronitrile 0.5% pet.	3+	1+
Benzisothiazolinone 0.1% pet.	1+	Negative
Tribenoside 5.0% pet.*	3+	ND
Tribenoside 2.5% pet.*	3+	ND
Tribenoside 1.0% pet.*	2+	ND
Tribenoside 0.1% pet.*	1+	ND
Tribenoside 0.01% pet.*	Negative	ND
Tribenoside 5.0% ac.*	3+	ND
Tribenoside 2.5% ac.*	3+	ND
Tribenoside 1.0% ac.*	3+	ND
Tribenoside 0.1% ac.*	2+	ND
Tribenoside 0.01% ac.*	2+	ND
Benzoic acid 5.0% pet.*	3+	ND

Note: Occlusion time 24 h; pet., petrolatum, ac, acetone, ND, not done.
*test was removed after 24 hrs and only one reading performed.

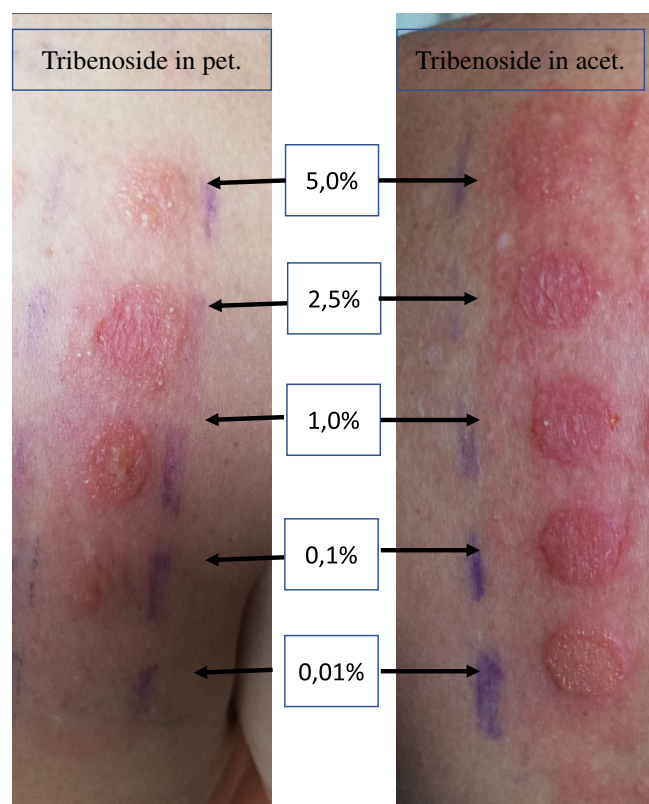


FIGURE 2 Positive patch tests reactions to tribenoside in petrolatum (pet.) and acetone (acet.) in serial dilutions

Pharmacopoeia [EP] Reference Standard, Sigma-Aldrich, Darmstadt, Germany) in acetone and pet. (Table 1). Patches were removed after 24 hours because of the severe itching. Positive reactions occurred to benzoic acid and all concentrations of tested tribenoside with the exception of 0.01% pet. (Figure 2).

Based on the clinical history and the results of the patch tests, a diagnosis of allergic contact dermatitis to tribenoside was confirmed. As the patient did not experience any adverse reactions from the contact with other substances tested positive, other contact allergies were considered as of unknown clinical relevance.

DISCUSSION

Tribenoside (ethyl-3,5,6-tri-O-benzyl-D-glucopyranoside, CAS-No. 10310-32-4) has been described as a vasoprotective substance with a wide spectrum of activities (anti-inflammatory, mild analgesic, etc.).¹ In combination with lidocaine it is used as a rectal crème or suppositories in treating haemorrhoids, and in the EU it is an over-the-counter drug. Around 20% of the administered tribenoside is metabolized to benzoic acid¹ and this could explain positive reactions to other substances containing benzoic acid (eg, in *Myroxylon Pereira*).² As benzoic

acid does not accumulate in the plasma some speculate that it is not the main allergen formed from tribenoside.^{3,4} However, the concomitant reaction to benzoic acid in our case rather favours the theory that benzoic acid is the true hapten of tribenoside.¹

Using serial dilutions often helps to interpret the test reactions, especially with rare or unknown allergens. In one previously published case report,⁵ patch testing was performed using tribenoside 1% pet. and 5% pet., both concentrations resulting in 3+ reactions. We tried to pinpoint the lowest concentration of tribenoside eliciting a positive response and found that the safest concentration to test it is 0.1%–1.0% pet. Patch test reactions in acetone were stronger and it was impossible to find the lowest limit for the positive test.

To conclude, benzoic acid could be the main allergen formed from tribenoside, a rare contact allergen found in an over-the-counter drug, inducing contact allergy.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Kestutis Černiauskas: Investigation (equal); methodology (equal); validation (equal). **Linas Griguola:** Data curation (equal); investigation (equal); methodology (equal). **Anzelika Chomiciene:** Methodology (equal); project administration (equal); supervision (equal); validation (equal).

ORCID

Laura Malinauskienė  <https://orcid.org/0000-0002-3255-7669>

REFERENCES

1. Kestránek J. Hemorrhoid management in women: the role of tribenoside + lidocaine. *Drugs Context*. 2019;8:212602.
2. Aerts O, Goossens A. Contact allergy to preservatives. In: Johansen JD, Mahler V, Lepoittevin JP, Frosch PJ, eds. *Contact Dermatitis*. Cham, Switzerland: Springer; 2021.
3. Endo H, Kawada A, Yodate T, Aragane Y, Yamada H, Tezuka T. Drug eruption due to tribenoside. *Contact Dermatitis*. 1999;41(4):223.
4. Sioufi A, Pommier F. Biotransformation of tribenoside into benzoic acid in man. *Eur J Drug Metab Pharmacokinet*. 1982;7(3):223-228.
5. Inoue A, Tamagawa-Mineoka R, Katoh N, Kishimoto S. Allergic contact dermatitis caused by tribenoside. *Contact Dermatitis*. 2009;60(6):349-350.

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