



## **Finally an evidence-based indication for injectable phloroglucinol!**

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## **Finally an evidence-based indication for injectable phloroglucinol!**

Short title: **Phloroglucinol and povidone-iodine stains**

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The authors declare no conflicts of interest

## **Abstract**

**Background:** While phloroglucinol is widely prescribed in European countries for its antispasmodic properties, recent high quality data failed to demonstrate its superiority to placebo in alleviating abdominal pain. Rumors suggest that injectable presentation of phloroglucinol may erase povidone-iodine stains. We thus aimed to evaluate its efficacy in this new indication.

**Methods:** In this double-blind, controlled trial, we randomly assigned 9 squares of fabric obtained from common white coat to receive injectable phloroglucinol (experimental arm), stain remover (Eau Ecarlate, active control arm) or water (placebo arm). The primary efficacy endpoint was the change in stain intensity 10 minutes after the intervention.

**Results:** In placebo and active control arms, povidone-iodine stains remained unchanged 10 minutes after treatment application. In contrast, the stain disappeared completely in the experimental arm.

**Conclusion:** Injectable phloroglucinol was more effective than usual stain remover and water to remove povidone-iodine stains from white coats.

**Keywords**

Injectable phloroglucinol, povidone-iodine, stain, efficacy, randomized controlled trial.

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## **Introduction**

Just like Newton's falling apple revealed gravity to the scientific community, we recently had a life changing experience leading to a new indication for injectable phloroglucinol. Phloroglucinol is a phenolic compound, first prepared from phloretin in the nineteenth century. It shows a variety of biological activities and it is widely used in many fields such as pharmaceuticals, cosmetics, dyeing, pesticides and explosives. In medicine and particularly in gynecology, it is mostly used for its antispasmodic properties. However, its true efficacy is highly controversial. Indeed, a recent meta-analysis concluded that phloroglucinol was not superior to placebo in alleviating abdominal pain [1]. Nevertheless phloroglucinol is widely prescribed in European countries and has an important cost for health services: more than 9 million euros were spent in France in 2016 to reimburse these prescriptions [2]. Hence we came to the conclusion that phloroglucinol must have hidden invaluable properties.

Rumors suggest that injectable phloroglucinol can erase povidone-iodine stains. It seems like a solid hypothesis for these massive prescriptions, so we decided to further investigate this phenomenon.

Our primary objective was thus to compare the efficacy of injectable phloroglucinol with classic stain remover, in removing povidone-iodine stains from white coats.

## Methods

In this double-blind, randomized controlled trial, we compared phloroglucinol at a concentration of 10mg/mL with classic stain remover and with placebo.

We cut a white coat into 9 squares of fabric measuring 225 cm<sup>2</sup>. Then, they were stained with two milliliters of povidone-iodine. Each square of fabric was randomly assigned to receive injectable phloroglucinol (experimental arm), stain remover (Eau Ecarlate, active control arm) or water (placebo arm). An independent comity prepared the blinded vials, each containing 8 mL of solution. All solutions were transparent and had no smell. Neither the participants (coats) nor the investigators were aware of the trial-group assignments. The assessed treatment was applied directly on the stain and left on for 10 minutes. Each square of fabric was placed on a white table, under the same light, at the same time of day, and photographed at baseline and 10 minutes after treatment application.

The experiment was performed in triplicates.

Our primary outcome was the intensity of the stain after the intervention.

Secondary outcomes were: recovery of the initial color, damaging of the fabric.

## **Results**

The experiments took place at Purpan Hospital, Toulouse, France in February 2019.

In placebo and active control arms, povidone-iodine stains remained unchanged 10 minutes after treatment application. In contrast, the stain disappeared completely in the experimental arm (Figure 1-A). Furthermore, phloroglucinol application did alter fabric native color (Figure 1-B). Last, none of the fabrics were damaged by allocated treatments.

At the end of the experiment, all fabrics were washed in a laundry machine with common detergent (30°C for 30 minutes). All stains disappeared.

In order to demonstrate the external validity of our findings, we repeated the experiment with different fabrics. The results were similar.

## Discussion

In this experiment, we found that injectable phloroglucinol was more effective than usual stain remover and water to remove povidone-iodine stains from white coats.

Phloroglucinol (1,3,5-benzenetriol) is a phenolic compound. Two forms have been described: 1,3,5-trihydroxybenzene and 1,3,5-cyclohexanetrione. Povidone-iodine is a stable chemical complex of povidone, elemental iodine and hydrogen iodide. It is widely used as antiseptic, especially in operating rooms. That's why white coats are often stained with povidone-iodine. As demonstrated above, povidone-iodine stains are very hard to clean, and classic stain remover is not efficient. Indeed, such stains are an everyday life issue for medical staff. It particularly affects obstetricians: it is well-known that they are very clumsy surgeons, therefore they often find themselves with such stains on their coats. Supporting why phloroglucinol is the most frequently used medication in maternity wards.

Besides their negative effect on practitioners' style of dress, povidone-iodine stains may also drive a financial impact through the waste of white coats. We now have a very simple solution to avoid this enormous misuse of money. Given the financial difficulties of French hospitals, we believe this information should be widely spread.

Whilst enlightening, this experiment leaves unanswered questions. For instance, povidone-iodine stain can be on a pocket of the white coat. That is even harder to clean because of the double layer of fabric. Other trials should be conducted to test the efficacy of phloroglucinol in different conditions.

## References

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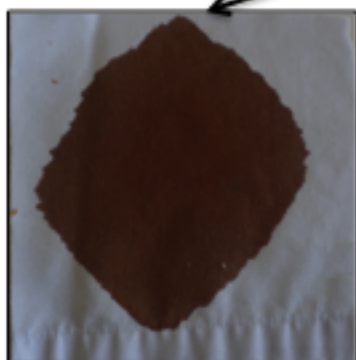
2- Medic'AM (2016) Données mensuelles et annuelles sur les médicaments remboursés par l'Assurance Maladie. <https://www.ameli.fr/l-assurance-maladie/statistiques-et-publications/donnees-statistiques/medicament/medic-am/medic-am-mensuel-2016.php>. [1<sup>er</sup> SEP]

## **Figures captions**

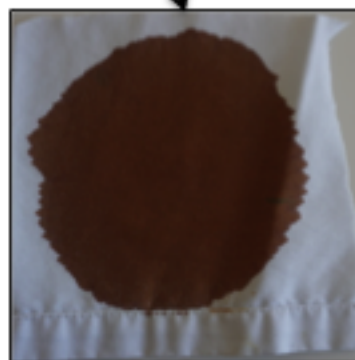
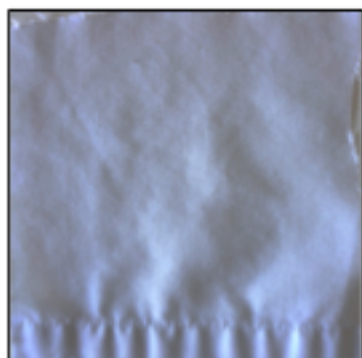
Figure 1. A- Comparative outcome in stain intensity according to treatment arms; B- Impact of phloroglucinol treatment on native color of the fabric

4ml povidone-iodine

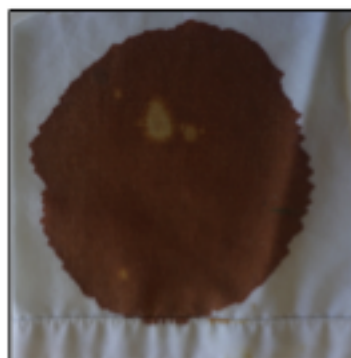
Baseline



8ml phloroglucinol



8ml stain remover



8ml water



10 minutes