

# Double-blind, placebo controlled, randomized study of Z-Gel

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## SUMMARY

This randomized study, double-blind, placebo-controlled, demonstrates that Z-Gel All-Purpose Soothing Gel (names Z-Trauma in France) reduces the pain killer tablet's consumption by 32% and decreases hematomas size after surgery by 41% in comparison to a placebo gel after a similar vascular surgery (crossectomy, stripping, phlebectomy).

These representative results demonstrated that Z-Gel is an efficient post surgery comfort product allowing a faster return to validity improved by the surgery.

## CONTEXT AND METHOD

For several years, scientists (physicist and pharmacist) have worked on a comfort cream called Z-Gel (Z-Trauma in France). Having very good returns using this gel, the Montreal private clinic of Carcassonne proposed at the Mint-e Health laboratory (producing Z-Gel) to undertake a double-blind clinical study in order to scientifically check the effects of the gel after a vascular surgery which is known to generate pain and severe hematomas.

This study was undertaken within the vascular department surgery of Dr. Sala at the Montreal private hospital of Carcassonne.

**Objectives:** To check if Z-Gel, using extracts of plants like the arnica, calendula, plantain, horsetail, blackcurrant and propolis as well as floral elixirs into postoperative (crossectomy, stripping, phlebectomy), is an efficient comfort product, we realized between 2007 and 2008, a double blind randomized test against a placebo. Our aim is to show that the subtle synergy between plants in the gel is making Z-Gel a post-surgery product of comfort that supports well-being.

**History:** Allegations were made, thanks to the ingredients of this organic certified gel, that Z-Gel is soothing pain with an anti-inflammatory action and anti-bruise action. Z-Gel is seeing as a comfort product increasing post-surgery well-being. Its ingredients have the following medicinal uses:

INGREDIENTS	Evidence of benefit (reference)
MEADOWSWEET	Anti-inflammatory, antiseptic, aromatic (2), (3)
ARNICA	Bruises and sprains (1)
CALENDULA	Wound healing (4) (5) Sunburn (6) Irritated skin (7)
PLANTAIN	Wound healing (8) Inflammatory skin reactions (9)
HORSETAIL	Hemostyptic (helps stops bleeding). Wound healing (10)
SILICA	Wound healing (11)
BLACKCURRANT	Anti-inflammatory (12)
ETHANOL	Antibacterial (13)
PROPOLIS	Antiseptic, antimicrobial (14)
GRAPEFRUIT EXTRACT	Antibacterial, antifungal (15)
CARAGEENAN	Potential infection inhibitor (16)
VEGETABLE GLYCERIN	Emollient properties (17)
FLOWER ESSENCES	Emotional imbalances (18)

**Method:** 40 patients, men and women, ages varying between 37 and 81 years, have participated in this randomized double blind study with a control placebo. No member of the private clinic could differentiate Z-Gel from the placebo: same texture, even odor. We had 2 pools of 20 for Z-Gel and the Placebo.

An initial questionnaire was filled out by the patient in order to evaluate his health, its score of pain before and after the surgery, its pain killers use and its emotional level. Another questionnaire was reserved to the hospital staff in order to follow the evolution pre/post surgery. The data is distributed according to Normal law; we will use statistics parametric tests with a risk  $\alpha$  of 5 %.

The studied values are:

- The number of pain killer tablets taken every day after the surgery
- Size of the hematomas (bruises) measured one week after the surgery

## Scientific reasoning:

We wanted to compare averages between two independent samples Z-Gel and Placebo with respectively  $n=20$  thus  $n < 30$ .

For the comparison of average “number tablets/day” into postsurgery, we are choosing a risk  $\alpha$  of 5%.

Two major assumptions have to be made:

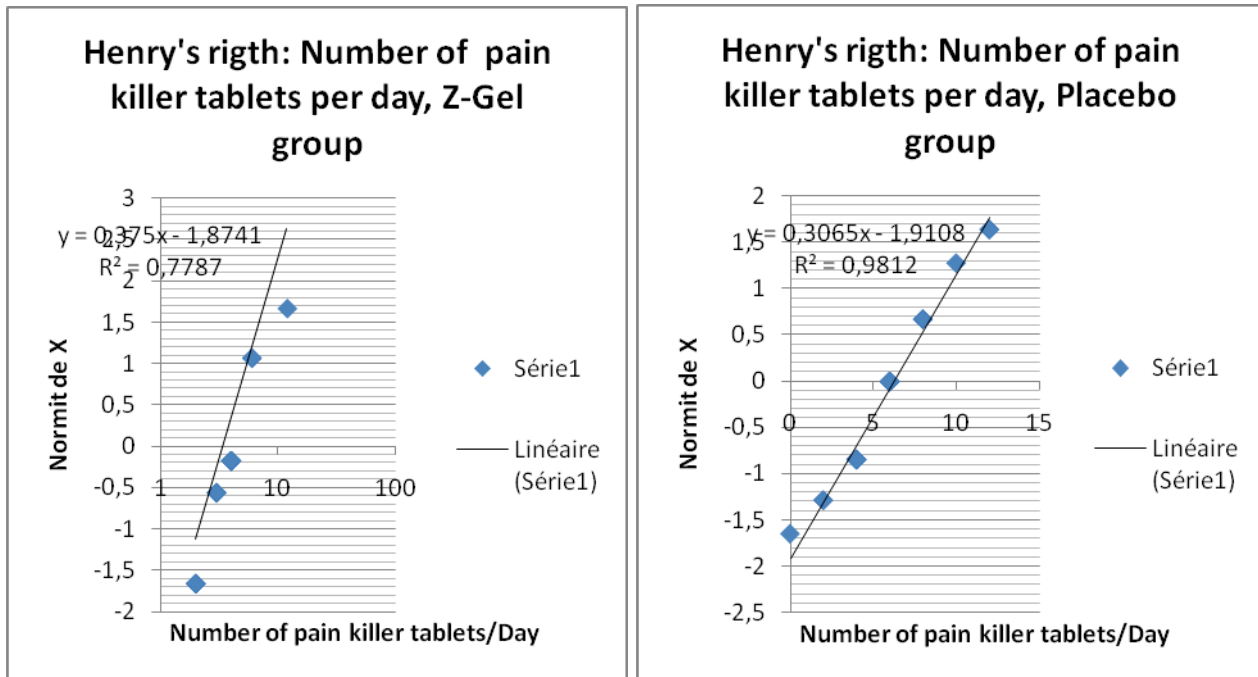
- Variable X is distributed according a Normal law for the two samples (Henry’s line)
- Equality of the variances

The null hypothesis ( $H_0$ ) was that there would be no significant differences between Z-Gel and Placebo groups.

## Normality of variable X distribution

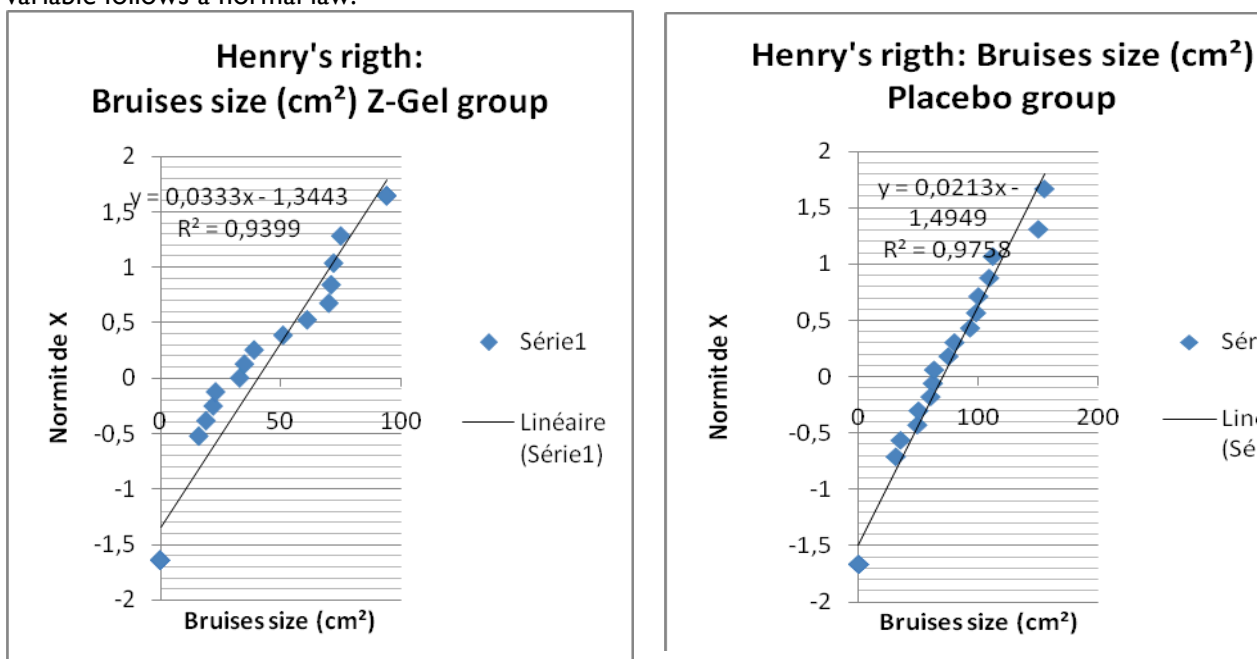
### a) The number of pain killer tablets per day

In order to demonstrate that variable X is distributed according to a Normal law, we draw a line of Henry calculating the cumulated number of patients, the cumulated frequency and the Normit of X. (graphic below). This variable follows obviously a Normal law.



### b) Hematoma Size one week after the surgery

To show that variable X is distributed according to a normal law, we drawn a straight line of Henry by calculating cumulated number of patients, the cumulated frequency and the Normit of X. (graphic below). This variable follows a normal law.



## Significant variances and averages

### a) The number of Pain killers' tablets per day

The next stage will be to check if the variance of the two groups is identical. For that purpose, we conducted a test of Fisher based on the calculation of F of Snedecor ( $F > 1$ ). In our case  **$F = 2.013691417$** .

With a  $F_{5\%}$  in the Snedecor table with a degree of freedom,  $ddl = n-1 = 19$ , our value in the table is  **$F_{5\%} = 2.53$** .

We thus have  $F < F_{5\%}$ , therefore this is null assumption  $H_0$  showing that there are no significant differences, therefore we have identical **variances** between the two groups of patients.

This assumption being now confirmed, if we calculate the common variance  $S^2$ , we have  $S^2 = 7.530263158$ , and the standard deviation  **$E = 2.131899126$** .

In the Student Table,  $E_{5\%}$  with a  $ddl = n_1 + n_2 - 2 = 38$  we find  **$E_{5\%} = 2.04$** .

Because we have an  $E > E_{5\%}$ , we are thus on the alternative assumption  $H_1$  that there is a **significant and representative difference of the number of pain killer tablets per day averages** taken during post-surgery between the two groups.

### b) Hematoma size one week after surgery

Same method, the next stage will be to check if the variance of the two groups is identical. For that purpose, we conducted a test of Fisher based on the calculation of F of Snedecor ( $F > 1$ ). In our case  **$F = 2.098539233$**

With a  $F_{5\%}$  in the Snedecor table with a degree of freedom,  $ddl = n-1 = 19$  is of  **$F_{5\%} = 2.53$** .

We thus have an  $F < F_{5\%}$ , therefore a null assumption  $H_0$  showing that there are no significant differences, therefore we have identical **variances** between the two groups of patients.

This assumption being now confirmed, if we calculate the common variance  $S^2$ , with  $S^2 = 1645.303947$  and the standard deviation  **$E = 2.131899126$** .

In the Table of Student,  $E_{5\%}$  with a  $ddl = n_1 + n_2 - 2 = 38$  we find  **$E_{5\%} = 2.04$** .

Because we have an  $E > E_{5\%}$ , we are thus on the alternative assumption  $H_1$  that there is a **significant and representative difference of the number of bruise size averages** taken during post-surgery between the two groups.

## RESULTS:

The patients' distribution included in the clinical trial is shown in table I. Of the 66 patients recruited for the clinical trial, 40 are included in the statistical analysis. The flow of patients through the trial is displayed in FIGURE I.

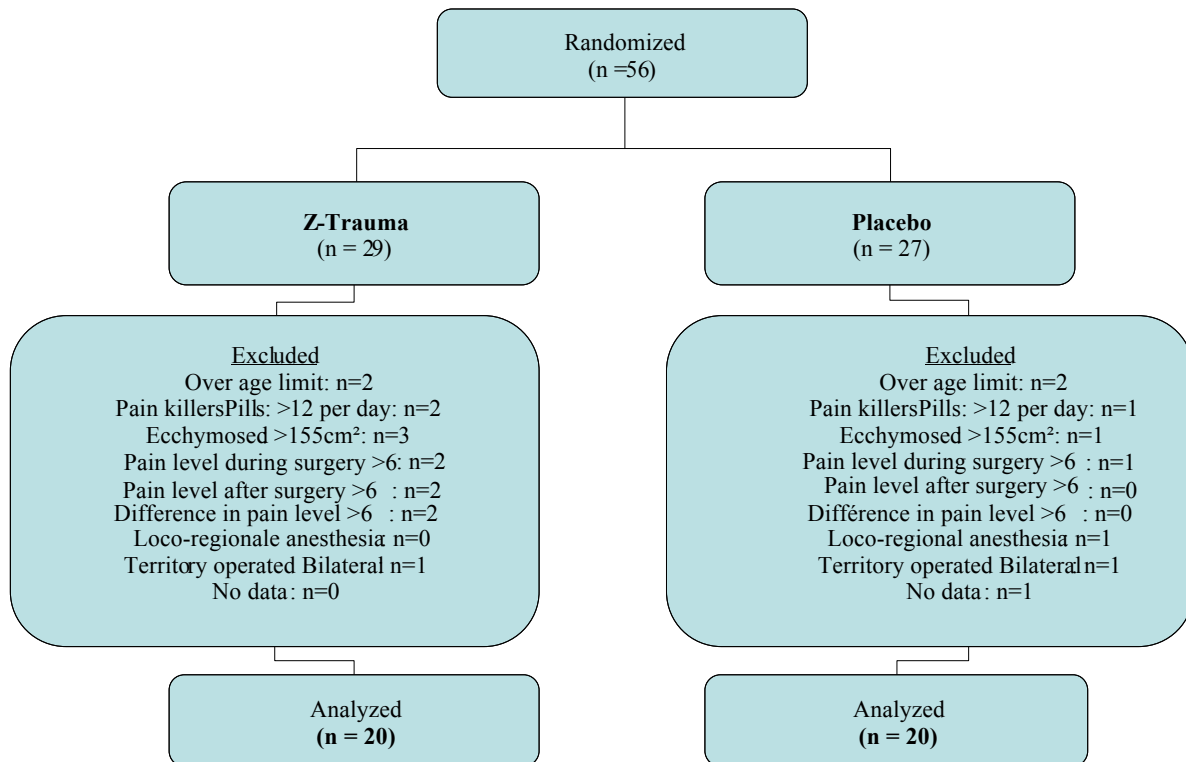


Figure I: Trial flow

### Criteria of exclusion:

- Age between 37 and 81 ans
- Pain killers tablets > 12/

Beyond 12 pain killer tablets a day taken after surgery we are not in the scope of a comfort soothing cream.

- Bruises > 155cm<sup>2</sup>

Beyond bruise size of 155cm<sup>2</sup> after surgery, we are not in the scope of a comfort soothing cream.

- Pain level during surgery > 6
- Pain level during surgery > 6
- Difference in pain level > 6

When the pain level is too high, we don't integrate these patients into the study.

- Loco-regional anesthesia

The person was too weak to undergo an assisted local anaesthesia, weighing only 38 kg; this is why we have excluded her from the study.

- Territory bilateral surgery

Too heavy surgery for the study of a comfort soothing cream and difficult to compare the results with the others.

We can see similarities in the characteristics of the patients of the 2 groups for several data like age, the weight, the size. However, the placebo group contains more women than men compared to the Z-Gel group. (Table 1)

	<b>Z-trauma (n=20)</b>	<b>Placebo (n=20)</b>
<b>M/F</b>	4/16	10/10
<b>Age [years]</b>	50,46	57,66
<b>Weight (Kg)</b>	71,33	74,82
<b>Height (cm)</b>	164,27	168,23

Table 1: Patients characteristics

Respectively there is a significant difference between the two groups Z-Gel and placebo for the studied data. We can note a clear improvement of the bruises size and a lower number of pain killer tablet per day taken during post-surgery.

With  $p < 0,05$ , our data demonstrates a significant difference with a risk  $\alpha$  of 5% between the averages of pain killer tablets taken into post-surgery. The average of pain killer tablets taken into post-surgery with **Z-Gel is 3.95 tablets with Z-Gel against 5.8 tablets per day with the placebo**. This equates to a **32%** reduction of pain medication for patients in the Z-Gel group.

In addition, with  $p < 0,05$ , we have a significant difference with a risk  $\alpha$  of 5% between the averages of the bruises size between the two groups. The average of bruises ( $\text{cm}^2$ ) in postoperative will be **38.75  $\text{cm}^2$  with Z-Gel against 66.1  $\text{cm}^2$  with the placebo**. There is a significant **difference of 41%** in the bruises size between the two groups. (Table 2)

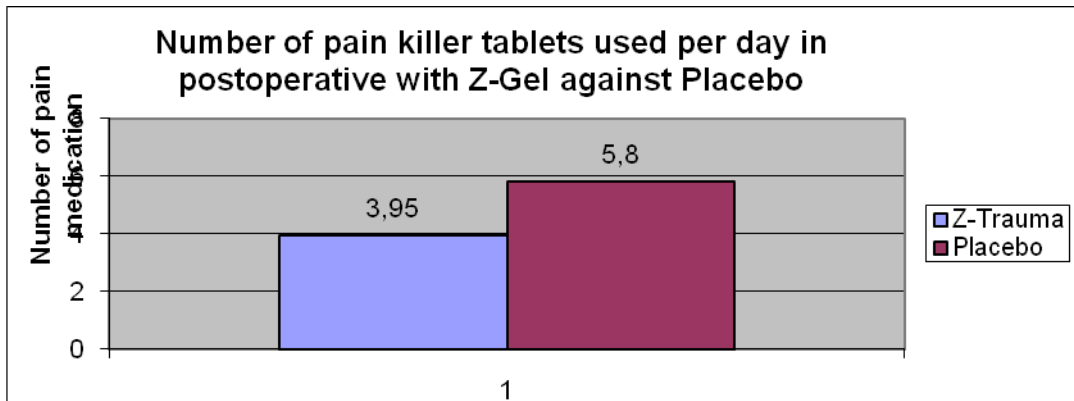
	<b>Z-trauma (n=20)</b>		<b>Placebo (n=20)</b>	
	<b>Average</b>	<b>Standard deviation</b>	<b>Average</b>	<b>Standard deviation</b>
<b>Bruises size (<math>\text{cm}^2</math>)</b>	38.75	32.59	66.1	47.21
<b>Number of pain killer tablets per day</b>	3.95	2.24	5.80	3.17

Tableau 2: Averages and standard deviations of the surface of the bruises in  $\text{cm}^2$  and the number of pain killer tablets used per day into post-surgery

## DISCUSSION:

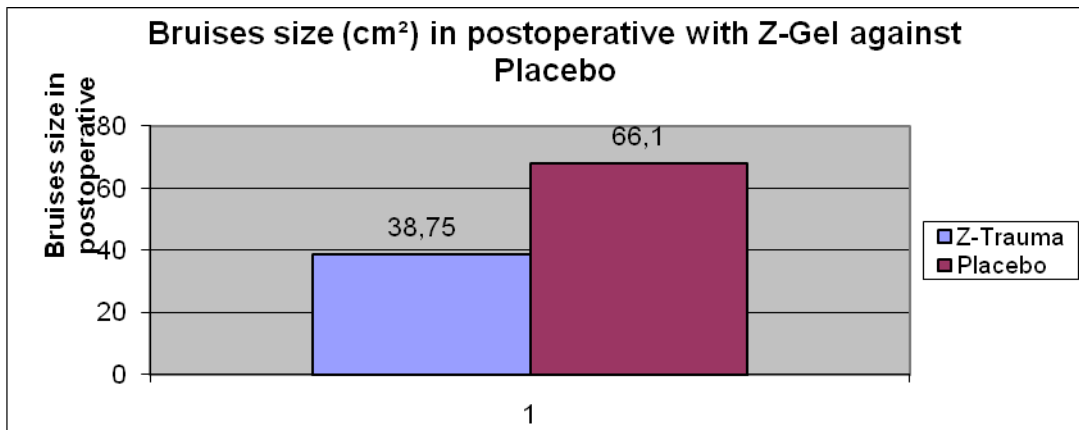
Z-Gel obtained better results than the placebo in post-surgery for the support of the pain treatment as well as the reduction of bruises sizes. Z-Gel is improving the overall patients well-being.

With a 32% reduction of the number of pain medication taken during post-surgery with Z-Gel compared to the placebo. These significant results enable us to put forward the anti-inflammatory known properties of calendula, plant ago major and blackcurrant (Graph 1).



Graph 1: Number of pain killer tablets used during post-surgery for the 2 groups Z-Gel and placebo

While referring to the results we note a significant 41% reduction in the bruises size between the 2 groups. This result is due to the arnica known anti-bruises properties (Graph 2).



Graph 2: Bruises Size in cm<sup>2</sup> into postoperative with Z-Gel against the placebo

However it also should be noted that the two groups were not identical regarding their level of pain. In the questionnaire we have checked pain's levels in a scale from 0 to 10 before and after surgery.

The pain level average before the intervention is 1.95/10 for the Z-trauma group and 1.25/10 for the Placebo group.

This average after surgery stay identical for Z-Gel group with 1.95/10 while with Placebo the average of pain level had increased to 2.7/10.

These figures imply that using Z-Gel people have an identical level of pain before and after the surgery, whereas with the Placebo this level of pain increases.

Z-Gel thus is an effieied comfort gel which allows a faster return to validity improved by the surgery.

## Conclusion :

This randomized double-blind study demonstrates a significant difference using the risk of 5% between the Z-Gel and placebo groups for anti-pain and anti-bruises, which enables us to say that Z-Gel is a comfort product which can be used effectively into postoperative after crosssection, stripping, phlebectomy.

This is in line with a cosmetic action: Serving to modify or improve the appearance of a physical feature, defect, or irregularity. Z-Gel being a simple topical cosmetic topical cream.

The surgery can solve the cause of the problem but, as the study showed, more comfort and less pain are synonymous of a faster return to validity.

## Potential Generalization :

One can expect that Z-Gel can also improve a post surgery comfort in the cases of:

- Plastic and cosmetic surgery
- Orthopedics surgery

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