Clinical evaluation of the efficacy of an anti-aging product on skin hydration, in 20 women volunteers, after single application at T+2H, T+4H, T+6H, T+24H and T+48H

STUDY REPORT 17E3961

Quote D17-656-2

Study performed on:

- **20 Caucasian women**
- **Reference :**

Rivoli crème de jour Jeunesse II
Torstone
Lab-01095.4
14/12/17

Study report transmitted by BIO-EC, on March 2nd, 2018

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QUOTE D17-656-2	
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Summary of the study

TITLE:

Clinical evaluation of the efficacy of an anti-aging product on skin hydration, in 20 women volunteers, after single application at T+2H, T+4H, T+6H, T+24H and T+48H

AIM OF THE STUDY:

The aim of the study is to assess objectively the efficacy of an anti-aging product on the cutaneous hydration by biometrological measurement.

This efficacy will be measured on forearm through the assessment of cutaneous hydration by Corneometer® CM825TM (Courage&Khazaka). It was a single-blind monocentric study.
The different measures were performed at T0 and then at T+2 hours, T+4 hours, T+6 hours, T+24 hours and T+48 hours after application of the product.

PROGRESS OF THE STUDY:

20 women, aged between 18 to 65 years old, meeting the inclusion and non-inclusion criteria defined by the promoter were included in the study.

Inclusion criteria:

- Without hot flush
- With a dry skin on the forearm
- With a corneometry value <40 on the forearm
- Without scars, wound or hair on the inner side of the arm
- Having to wash the measurement areas in the morning with water only

The measurements were taken in a controlled-atmosphere room (temperature: 20°C ± 1°C; hygrometry: 45% HR ± 5%), after stabilization of the volunteers for at least 30 minutes. Each volunteer stayed two hours in the laboratory.

- **Product :**

Single standardized application of the product by a technician of BIO-EC on previously defined areas on the inner face of the forearm (2mg/cm²).

- **RESULTS AND CONCLUSION:**

The aim of the study is to assess objectively the efficacy of an anti-aging product on the cutaneous hydration by biometrological measurement.

In conclusion:

- **there is no site effect at the initial time point (T0)**
- **2 hours after application of the product, we can observe a significant increase of skin hydration**
- **4 hours after application of the product, we can observe a significant increase of skin hydration**
- **6 hours after application of the product, we can observe a significant increase of skin hydration**

INTRODUCTION

1. STUDY DESIGN

1.1. Study objective

The aim of the study is to assess objectively the efficacy of an anti-aging product on the cutaneous hydration by biometrological measurement according to the protocol D17-656-2.

1.2. Study type

This study is a kinetic of hydration at T0, T+2 hours, T+4 hours, T+6 hours, T+24 hours and T+48 hours with the Corneometer® on 20 volunteers.

1.3. Principle

This efficacy will be measured on forearm through the assessment of cutaneous hydration by Corneometer® CM825TM (Courage&Khazaka). It was a single-blind monocentric study.
The different measures were performed at T0 and then at T+2 hours, T+4 hours, T+6 hours, T+24 hours and T+48 hours after application of the product.

1.4. Investigational product

The product was identified as follow:

Rivoli crème de jour Jeunesse II
Torstone
Lab-01095.4
14/12/17

The product was stored at room temperature.

The product was a white cream packed in opaque white vials by the promoter.

The product was applied by the technician on area defined on forearm at 2mg/cm².

1.5. Subjects

- **Real inclusion criteria**

- Caucasian women having between 32 and 60 years old
- Informed and consenting patients who have undergone a general clinical examination attesting to their ability to participate in the study
- Without hot flush
- With a dry skin on the forearm (corneometry value <40)
- Without scars, wound or hair on the inner side of the arm

- **Real non inclusion criteria**

- Pregnant or breastfeed women
- Having applied a cosmetic or pharmaceutical product other than the usual cleaner during the 72 hours preceding the study at the level of the arms
- Showing signs of recent and intense sun or UV exposure
- Suffering from systemic diseases or any dermatitis likely to interfere with the study according to the investigator's assessment
- Subjects with dermatological problems and/or known allergy to cosmetic products and/or to one of the cream constituents,
- Participating in another study or being in an exclusion period from another study

- **Volunteers included in the study**

Overall, 20 volunteers, meeting the inclusion and non-inclusion criteria defined on the protocol, were included in the study. They were informed of the possible adverse effects from using the product and the technical conditions in which the assessment is performed. They willingly signed the consent form which was written in compliance with the Declaration of Helsinki and the December 20th, 1988 act of the Code de la Santé Publique.

- **Planning of the study**

- **Recruitment** (Week 3): Women having between 32 to 60 years with dry skin on forearms (corneometry value <40)

- **First visit at T0** (22 and 24.01.2018) :

The technician in charge of the study,

- Makes stabilize the volunteer on a control atmosphere room during 30 minutes,
- Checks out of the criteria of inclusion and non inclusion,
- Signing of the agreement by the volunteers,
- Delimits 2 area (13cm²) on the forearm
- Makes initial biometrical measurements on forearm on area defined (Corneometer®),
- Includes or not the volunteer on the study,

A second technician,

- Applies the product on area defined on forearm at 2mg/cm².

- **From T0 to T+2hours:** Volunteers stay 2 hours on a control atmosphere room

- **Visit at T+2 hours** (22 and 24.01.2018) :

The technician in charge of the study,

- Records adverse events
- Makes biometrical measurements on forearm on area defined (Corneometer®)

- **From T+2hours to T+4 hours:** Volunteers stay 2 hours on a control atmosphere room

- **Visit at T+4 hours** (22 and 24.01.2018) :

The technician in charge of the study,

- Records adverse events
- Makes biometrical measurements on forearm on area defined (Corneometer®)

- **From T+4 hours to T+6 hours:** Volunteers stay 2 hours on a control atmosphere room

- **Visit at T+6 hours** (22 and 24.01.2018) :

The technician in charge of the study,

- Records adverse events
- Makes biometrical measurements on forearm on area defined (Corneometer®)

- **From T+6 hours to T+24 hours:** The volunteers do not wet their arms until the next morning

- **Visit at T+24 hours** (23 and 25.01.2018) :

The technician in charge of the study,

- Records adverse events
- Makes biometrical measurements on forearm on area defined (Corneometer®)

- **From T+24 hours to T+48 hours:** The volunteers do not wet their arms until the next morning

- **Final visit at T+48 hours** (24 and 26.01.2018) :

The technician in charge of the study,

- Records adverse events
- Makes biometrical measurements on forearm on area defined (Corneometer®)
- Gives compensation to volunteer

- **Deviation of the initial planning**

No deviation of the initial planning was made.

1.6. Methodology

The stratum corneum hydration causes changing in its electrical characteristics. The stratum corneum is like a dielectric corps. Any modifications of its hydration statement cause a variation of the electric capacity measured by a condenser. Higher is the hydration, higher is the electric capacity because its dipolar nature increases the electric permittivity of the environment and its conductibility.

Measurement is realized by the Corneometer CM825TM (Courage & Khazaka electronics). The probe linked to a condenser allows applying at all the time the same pressure on the tegument in order to not disturb the measures and to obtain good experimental conditions reproducibility.

1.7. Adverse event

No adverse effects occurred during the study.

1.8. Statistical analysis

Descriptive statistics will be provided for each parameter (effective, mean, mean difference, standard deviation, minimum and maximum) for each group at T0, T+2 hours, T+4 hours, T+6 hours, T+24 hours, T+48 hours, T2H-T0, T4H-T0, T6H-T0, T24H-T0 and T48H-T0.

The significance threshold will be set at 5% bilateral. The Student test or non-parametric Wilcoxon test are performed for paired data.

1.9. Interpretation of the results

	Forearm
Very dry skin	< 35
Dry skin	35 - 50
Sufficient hydration of the skin	> 50

2. REGULATION – CONFIDENTIALITY – LEGAL FORMALITIES

2.1. Regulations

This study is conducted on healthy volunteers, with non-invasive measurements, to whom cosmetic products with proven safety will be distributed.

Realisation of ethics of the study

This study will be conducted in full compliance with the principles of the Helsinki Declaration (amended in Tokyo, Venice, Hongkong, Somerset West, Edinbourg), with the local laws and regulations, governing clinical studies and with Good Clinical Practice (ICH E6 + decision from 24 November 2006 published in Official Journal on November 30, 2006).

Informing the volunteers

A preliminary meeting of study investigator and a volunteer ensures a good informing of the volunteer. During the meeting, the volunteer is informed about the nature, the goal, the duration, the method, the expected benefits, the constraints, the inconveniences and the risk involved, if there is some. The volunteer is also informed about his/her right to refuse the participation as well as about his/her right to withdraw from the study at any moment.

The products are provided for free by the Promoter.

Insurance and compensations

Liability insurance is contracted by L'OREAL covering its responsibility to the study.

In the case of a problem with general health, caused by the participation of the subjects in the study, the subjects receive compensation in accordance with the current legislation.

Protection of the rights of patients

The staff of the Promoter should strictly respect the rights of patients. For the monitoring of the study and the inspection of the data, international procedures are applied (Good Clinical Practice). This ensures the consensual acceptance of the results of a study and involves both the possibility of their publication and their presentation at congresses.

On the basis of the patient consent, the data will be entered anonymously. The monitors will be held at complete discretion.

The experimenters, the investigators and any person who is involved in the study shall be bound by professional secrecy as regards all confidential information that they receive

concering the nature of the studied products, the study, the involved persons and the obtained results.

They are not allowed, without the permission of the Promoter, to give information related to the studies to anyone, except the Minister of Health, the doctors and pharmacists inspectors. The study should not become an object of any comments written or oral without the permission from the experimentator, or the investigator, or the Promoter.

2.2. Confidentiality

Any information obtained during the realisation of the protocol, its implementation and its conduct is confidential.
In compliance with the article R 5120 of the Public Health Code and the recommendations of the Ministry of Health, the persons, participating in the presented study are informed about their duties related to the confidentiality.
In compliance with the article R 5120 of the Public Health Code, the study should not become an object of any commentaires written or oral (article, communication, poster...) without the permission from the investigator, or from the responsible of Laboratoire BIO-EC, or from the Promoter.

2.3. Legal formalities

The data that could be considered as being related to medical confidentiality will be preserved and retained according to the Good Clinical Practice. The data can be consulted only in accordance with the conditions governed by the Public Health Code.

The access to the total data, including the data considered as confidential data, is authorized to the audit demanded either by the Promoter or by the registration authorities. For this purpose, the consent of each subject will be specially demanded in the consent form before the start of the study. All the possible consultations with these data will be realized with the respect of their confidentiality.

Laboratoire BIO-EC will retain a copy of the protocol, signed by the Promoter, by the investigator and by itself in the Case Report Form, as well as the questionnaires of auto-evaluations. The investigator will retain all the elements serving to fill the Case Report Form, the consent forms signed by the subjects, the original documents of any nature and all the elements related to the project (appendixes).

All the documents will be stored for ten years, starting from the date of sending of the final report and will be available for all the inspections within a reasonable time limit by a representative, authorised by L'Oreal or by the supervisory authorities.

L'Oreal will be informed by each side about their intention to proceed to the destruction of the data after ten years of storage.

In compliance with the article 54 of the French data protection act of 06-01-1978 modified, the automated processing of the data (in the context of biomedical research) will be proceeded according to the reference methodology. In the consent form it will be indicated that the subject can excercise his/her right of the access at any moment from the investigator.

From the other part, at BIO-EC, all the digital data related to the study (data of measurements, documents related to protocols) will be securely stored and delocalized through the Adhersis Company via the system Backupia.

3. DATA RECORDING AND ARCHIVING

- **Raw data filing**

The raw data consists of:

- Image analysis results
- Assays results
- Biometrological results using devices

All the raw data is kept in a paper file and a backup is saved when it is possible (depending on the used device).

- **Products**

The products entrusted to BIO-EC are preserved one year after delivering the study report to the client.

- **Final report filing**

The paper file is archived and kept for 20 years. The study report (raw data, images, preliminary reports, final report) and all the computer data are saved thanks to a double internal backup (RISCBOX en RAID 1) and by an automated and daily external system, Backupia (RISC GROUP).

Our computer system is protected by the antivirus McAfee Saas.

4. RESULTS AND CONCLUSION

4.1. Amendements and protocol compliance

No volunteer left the study prematurely. All volunteers returned for their appointments. All inclusion and evaluation criterion were respected.

5.2 Studied population

The demographic characteristics of the volunteer group (mean + SD) are as follows:

Rivoli crème de jour Jeunesse II	N = 20 women
	Age : 51 + 8 years old

5.3 Results and conclusion

- **Statistical analysis**

Descriptive statistics and means ± SD of Corneometry values at T0, T+2hours, T+4hours, T+6hours, T+24hours and T+48hours for the delta of variation are gathered in the table below.

	n= 24	T0	T+2 hours	Delta of variation (T0 – T+2 hours)	Statistic
Product	**Min**	32,7	39,3	-2,4	/
	Max	60,9	73,7	19,7	/
	Median	44,3	56,0	11,8	/
	Mean	44,85	55,84	10,99	p-value < 0,001 ***
	SD	6,95	9,24	5,55	
Control	**Min**	26,5	25,3	-6,4	/
	Max	60,6	64,7	4,2	/
	Median	43,7	45,7	1,0	/
	Mean	44,76	45,01	0,25	p-value = 0,7008 ns
	SD	7,35	8,42	2,89	
Statistic		p-value = 0,9449 ns	/	p-value <0,001 ***	

 # Significatif p<0.1 ** Significatif p<0.05* ***Significatif p<0.01* ****Significatif p<0.001*

	n= 24	T0	T+4 hours	Delta of variation (T0 – T+4 hours)	Statistic
Product	**Min**	32,7	38,0	-5,7	/
	Max	60,9	66,3	18,0	/
	Median	44,3	51,7	7,0	/
	Mean	44,85	52,79	7,94	p-value < 0,001 ***
	SD	6,95	8,50	5,52	
Control	**Min**	26,5	27,3	-9,7	/
	Max	60,6	64,0	4,3	/
	Median	43,7	42,7	0,5	/
	Mean	44,76	44,78	0,02	p-value = 0,9824 ns
	SD	7,35	8,23	3,40	
Statistic		p-value = 0,9449 ns	/	p-value <0,001 ***	

 # Significatif p<0.1 ** Significatif p<0.05* ***Significatif p<0.01* ****Significatif p<0.001*

	n= 24	T0	T+6 hours	Delta of variation (T0 – T+6hours)	Statistic
Product	**Min**	32,7	34,3	-5,4	/
	Max	60,9	63,0	12,3	/
	Median	44,3	49,8	4,5	/
	Mean	44,85	49,79	4,95	p-value <0,001 ***
	SD	6,95	7,81	4,93	
Control	**Min**	26,5	26,3	-9,7	/
	Max	60,6	62,0	11,0	/
	Median	43,7	44,4	-0,3	/
	Mean	44,76	44,46	-0,30	p-value = 0,7644 ns
	SD	7,35	7,88	4,46	
Statistic		p-value = 0,9449 ns	/	p-value <0,001 ***	

 # Significatif p<0.1 ** Significatif p<0.05* ***Significatif p<0.01* ****Significatif p<0.001*

	n= 24	T0	T+24 hours	Delta of variation (T0 – T+24hours)	Statistic
Product	**Min**	32,7	33,3	-8,6	/
	Max	60,9	57,7	8,0	/
	Median	44,3	45,2	-0,6	/
	Mean	44,85	45,31	0,47	p-value =0,6825 ns
	SD	6,95	6,39	5,01	
Control	**Min**	26,5	26,0	-10,8	/
	Max	60,6	60,0	10,3	/
	Median	43,7	44,7	-0,9	/
	Mean	44,76	44,41	-0,35	p-value = 0,7861 ns
	SD	7,35	7,01	5,74	
Statistic		p-value = 0,9449 ns	/	p-value =0,2939 ns	

 # Significatif p<0.1 ** Significatif p<0.05* ***Significatif p<0.01* ****Significatif p<0.001*

	n= 24	T0	T+48 hours	Delta of variation (T0 – T+48hours)	Statistic
Product	**Min**	32,7	31,3	-7,7	/
	Max	60,9	59,3	12,6	/
	Median	44,3	47,9	-0,6	/
	Mean	44,85	45,93	1,08	p-value =0,4008 ns
	SD	6,95	7,51	5,62	
Control	**Min**	26,5	26,3	-9,4	/
	Max	60,6	69,3	17,0	/
	Median	43,7	45,9	-0,1	/
	Mean	44,76	45,43	0,67	p-value = 0,6224 ns
	SD	7,35	9,37	6,00	
Statistic		p-value = 0,9449 ns	/	p-value =0,6453 ns	

 # Significatif p<0.1 ** Significatif p<0.05* ***Significatif p<0.01* ****Significatif p<0.001*

- **Results**

Means ± SD of Corneometry values at T0, T+2hours, T+4hours, T+6hours, T+8hours, T+24hours, T+48hours and for the delta of variation are gathered in the table below. Individual values for each volunteer are presented in the appendixes.

n= 24	T0	T+2 hours	Delta of variation (T0 – T+2 hours)	Statistic
Product	44,85 ± 6,95	55,84 ± 9,24	10,99 ± 5,55	p-value < 0,001 ***
Control	44,76 ± 7,35	45,01 ± 8,42	0,25 ± 2,89	p-value = 0,7008 ns
Statistic	p-value = 0,9449 ns	/	p-value < 0.001 ***	

*# Significatif p<0.1 * Significatif p<0.05 **Significatif p<0.01 ***Significatif p<0.001*

- there is no significant difference between the product and the control at T0
- 2 hours after application of the product, we can observe a significant increase by **24%** (p<0.001) of the corneometry

n= 24	T0	T+4 hours	Delta of variation (T0 – T+4 hours)	Statistic
Product	44,85 ± 6,95	52,79 ± 8,50	7,94 ± 5,52	p-value < 0,001 ***
Control	44,76 ± 7,35	44,78 ± 8,23	0,02 ± 3,40	p-value = 0,9824 ns
Statistic	p-value = 0,9449 ns	/	p-value <0,001 ***	

*# Significatif p<0.1 * Significatif p<0.05 **Significatif p<0.01 ***Significatif p<0.001*

- 4 hours after application of the product, we can observe a significant increase by **18%** (p<0.001) of the corneometry.

n= 24	T0	T+6 hours	Delta of variation (T0 – T+6 hours)	Statistic
Product	44,85 ± 6,95	49,79 ± 7,81	4,95 ± 4,93	p-value < 0,001 ***
Control	44,76 ± 7,35	44,46 ± 7,88	-0,30 ± 4,46	p-value = 0,7644 ns
Statistic	p-value = 0,9449 ns	/	p-value <0,001 ***	

 # Significatif p<0.1 ** Significatif p<0.05* ***Significatif p<0.01* ****Significatif p<0.001*

- 6 hours after application of the product, we can observe a significant increase by **12%** (p<0.001) of the corneometry.

n= 24	T0	T+24 hours	Delta of variation (T0 – T+24 hours)	Statistic
Product	44,85 ± 6,95	45,31 ± 6,39	0,47 ± 5,01	p-value = 0,6825 ns
Control	44,76 ± 7,35	44,41 ± 7,01	-0,35 ± 5,74	p-value = 0,7861 ns
Statistic	p-value = 0,9449 ns	/	p-value = 0,2939 ns	

 # Significatif p<0.1 ** Significatif p<0.05* ***Significatif p<0.01* ****Significatif p<0.001*

- 24 hours after application of the product, we don't observe significant variation of the corneometry.

n= 24	T0	T+48 hours	Delta of variation (T0 – T+48 hours)	Statistic
Product	44,85 ± 6,95	45,93 ± 7,51	1,08 ± 5,62	p-value = 0,4008 ns
Control	44,76 ± 7,35	45,43 ± 9,37	0,67 ± 6,00	p-value = 0,6224 ns
Statistic	p-value = 0,1960 ns	/	p-value = 0,6453 ns	

 # Significatif p<0.1 ** Significatif p<0.05* ***Significatif p<0.01* ****Significatif p<0.001*

- 48 hours after application of the product, we don't observe significant variation of the corneometry.

- **Conclusion**

The aim of the study is to assess objectively the efficacy of an anti-aging product on the cutaneous hydration by biometrological measurement.

In conclusion:

- **there is no site effect at the initial time point (T0)**
- **2 hours after application of the product, we can observe a significant increase of skin hydration**
- **4 hours after application of the product, we can observe a significant increase of skin hydration**
- **6 hours after application of the product, we can observe a significant increase of skin hydration**

Appendixes

1. PANEL DATA

VOL	AGE
1	55
2	38
3	57
4	42
5	59
6	59
7	49
8	52
9	32
10	58
11	51
12	57
13	58
14	53
15	48
16	39
17	39
18	52
19	54
20	60
Moyenne	50,6
Ecart type	8,3

LABORATOIRE BIOEC

Clinical evaluation of the efficacy of an anti-aging product on skin hydration, in 20 women volunteers, after single application at T+2H, T+4H, T+6H, T+24H and T+48H.

TABLE OF RESULTS and STATISTIC

Product

	VALUES						DELTA VARIATION					% VARIATION				
Volunteers	**T0**	**T2h**	**T4h**	**T6h**	**T24h**	**T48h**	**T2h**	**T4h**	**T6h**	**T24h**	**T48h**	**T2h**	**T4h**	**T6h**	**T24h**	**T48h**
1	49	64	60	59	49	53	14,8	11,1	9,8	0,1	3,8					
2	38	53	51	47	42	39	14,9	12,9	8,9	3,9	1,2					
3	52	68	66	61	45	51	16,8	14,2	9,2	-6,5	-0,8					
4	49	55	52	50	46	48	6,7	3,7	1,7	-2,9	-0,6					
5	61	74	66	63	58	59	12,8	5,4	2,1	-3,2	-1,6					
6	35	40	40	34	33	31	5,6	5,3	-0,4	-1,4	-3,4					
7	44	58	48	46	48	50	14,5	4,2	2,5	3,9	6,2					
8	46	63	60	58	42	50	17,0	14,0	12,3	-3,7	4,6					
9	43	52	48	47	37	37	9,0	5,3	3,7	-6,0	-6,3					
10	42	60	56	52	45	50	17,7	14,0	10,0	3,3	8,0					
11	50	57	54	51	49	45	6,4	4,0	0,4	-1,6	-5,6					
12	39	53	49	50	41	39	13,4	9,7	11,0	2,0	-0,6					
13	40	51	49	47	48	48	10,7	9,0	7,3	8,0	7,7					
14	33	39	41	39	40	45	6,6	8,0	6,6	7,0	12,6					
15	38	48	44	42	40	36	9,7	6,0	4,3	2,3	-2,0					
16	47	67	65	58	55	52	19,7	18,0	11,0	7,7	4,7					
17	56	61	60	57	55	55	5,3	4,0	1,3	-1,3	-1,3					
18	48	54	51	46	40	43	6,0	2,7	-2,0	-8,6	-5,3					
19	44	41	38	38	42	36	-2,4	-5,7	-5,4	-1,7	-7,7					
20	45	59	58	49	53	53	14,6	13,0	4,6	8,0	8,0					
MEAN	**44,85**	**55,84**	**52,79**	**49,79**	**45,31**	**45,93**	**10,99**	**7,94**	**4,95**	**0,47**	**1,08**	**25%**	**18%**	**11%**	**1%**	**2%**
SD	**6,95**	**9,24**	**8,50**	**7,81**	**6,39**	**7,51**	**5,55**	**5,52**	**4,93**	**5,01**	**5,62**					
MIN	32,7	39,3	38,0	34,3	33,3	31,3	-2,4	-5,7	-5,4	-8,6	-7,7		**Variation moyenne (%)**			
MAX	60,9	73,7	66,3	63,0	57,7	59,3	19,7	18,0	12,3	8,0	12,6					
MEDIAN	44,3	56,0	51,7	49,8	45,2	47,9	11,8	7,0	4,5	-0,6	-0,6	**24**	**18**	**12**	**2**	**1**

CONTROL

	VALUES						DELTA VARIATION					% VARIATION				
Volunteers	**T0**	**T2h**	**T4h**	**T6h**	**T24h**	**T48h**	**T2h**	**T4h**	**T6h**	**T24h**	**T48h**	**T2h**	**T4h**	**T6h**	**T24h**	**T48h**
1	43	40	41	40	44	46	-3,1	-2,1	-3,4	0,9	2,9					
2	47	49	49	46	46	46	1,6	2,2	-1,4	-1,4	-1,4					
3	55	59	58	54	44	52	4,2	2,9	-0,8	-10,8	-3,1					
4	47	47	49	47	45	47	0,0	1,7	-0,3	-2,3	0,0					
5	61	65	64	62	53	59	4,1	3,4	1,4	-7,9	-1,9					
6	27	25	27	26	26	26	-1,2	0,8	-0,2	-0,5	-0,2					
7	44	45	42	40	46	49	1,7	-1,3	-3,3	2,4	5,4					
8	48	46	48	53	47	51	-1,7	0,0	5,6	-1,0	3,3					
9	42	39	38	38	39	37	-2,7	-3,4	-3,4	-3,0	-4,4					
10	43	44	42	41	46	44	0,7	-1,0	-1,7	3,0	1,0					
11	39	39	39	40	40	36	-0,3	0,0	0,7	0,4	-3,6					
12	38	39	38	49	42	42	1,6	0,3	11,0	4,0	4,6					
13	52	53	53	53	60	69	1,0	1,0	0,7	7,7	17,0					
14	37	38	41	39	47	45	1,0	4,0	1,4	10,0	7,4					
15	39	41	38	41	38	32	2,0	-1,3	1,4	-1,0	-7,0					
16	44	46	46	47	54	50	2,6	2,3	3,0	10,3	6,6					
17	49	50	51	47	48	48	1,0	2,0	-2,0	-0,7	-0,7					
18	53	46	43	43	43	43	-6,4	-9,7	-9,7	-9,7	-9,4					
19	43	38	37	35	37	37	-5,0	-5,7	-8,0	-6,0	-6,3					
20	46	50	50	49	44	49	4,0	4,3	3,0	-1,4	3,3					
MEAN	**44,76**	**45,01**	**44,78**	**44,46**	**44,41**	**45,43**	**0,25**	**0,02**	**-0,30**	**-0,35**	**0,67**	**1%**	**0%**	**-1%**	**-1%**	**1%**
SD	**7,35**	**8,42**	**8,23**	**7,88**	**7,01**	**9,37**	**2,89**	**3,40**	**4,46**	**5,74**	**6,00**					
MIN	26,5	25,3	27,3	26,3	26,0	26,3	-6,4	-9,7	-9,7	-10,8	-9,4					
MAX	60,6	64,7	64,0	62,0	60,0	69,3	4,2	4,3	11,0	10,3	17,0					
MEDIAN	43,7	45,7	42,7	44,4	44,7	45,9	1,0	0,5	-0,3	-0,9	-0,1					

Student test (p-value)					
Product					
T2h/T0	**T4h/T0**	**T6h/T0**	**T24h/T0**	**T48h/T0**	
3,55232E-08	3,59568E-06	0,0003	0,6825	0,4008	
Significativity	***	***	***	ns	ns

Student test (p-value)					
Product vs Control					
T0	**T2h/T0**	**T4h/T0**	**T6h/T0**	**T24h/T0**	**T48h/T0**
0,9449	3,06946E-09	5,08876E-07	1,71858E-05	0,2939	0,6453
Significativity	ns	***	***	***	ns	ns

Student test (p-value)					
Control					
T2h/T0	**T4h/T0**	**T6h/T0**	**T24h/T0**	**T48h/T0**	
0,7008	0,9824	0,7644	0,7861	0,6224	
Significativity	ns	ns	ns	ns	ns