EVALUATION OF HEMODYNAMIC RESPONSES TO AN INDUCED STRESS IN HEALTHY SUBJECTS AFTER LACTIUM® 300 MG OR PLACEBO CONSUMPTION

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This report is based on the data from clinical trial "A randomized, double blind, placebo controlled trial evaluationg hemodynamic responses to an induced stress in healthy subjects after Lactium® or placebo consumption" (Protocol Number 14310-IN, 2010)

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LIST OF ABBREVIATIONS

Abbreviations	Meaning
AFSSAPS	Agence Française de Sécurité SAnitaire des Produits de Santé (French Health Authority)
ANCOVA	Analysis of Covariance
BMI	Body Mass Index
CPP	Comité de Protection des Personnes (ethics committee)
CRA	Clinical Research Assistant
CRT	Clinical Research Technician
DBP	Diastolic Blood Pressure
Dx	Day x
GCP	Good Clinical Practice
HAD	Hospital Anxiety and Depression Scale
HRT	Hormone Replacement Therapy
ICH	International Conference on Harmonisation
ITT	Intention To Treat
Max	Maximum
Med	Median
Min	Minimum
N	Number
NA	Non Applicable
NR	Number of Randomization
NS	Number of Screening
PP	Per Protocol
SBP	Systolic Blood Pressure
SD	Standard Deviation

SEM	Standard Error of the Mean
STAI	State-Trait Anxiety Inventory
Tx	Time x
Vx	Visit x

Units	**Meaning**
a.u	arbitrary units
bpm	beats per minute
kg	kilogramme(s)
L	litre(s)
m	metre(s)
mg	milligramme(s)
mmHg	millimetre of mercury
nmol	nanomole(s)

1 Ethics

1.1 Authorities approval

The original protocol of this clinical study and its different amendments were approved by the CPP (ethics committee) Ouest IV of Nantes and the French Health Authority (AFSSAPS).

1.2 Regulation statement

The clinical study was carried out in accordance with the standards of Good Clinical Practice (GCP) for the evaluation of medical devices and medicinal products (ICH topic 6), the declaration of Helsinki and current French regulation (Code de Santé Publique, Titre II du livre Premier).

2 Study objectives

Main objective:

The main objective of the clinical was to determine the effect of Lactium® on the evolution of the systolic blood pressure (SBP) due to an induced stress after a consumption of 6 weeks.

Secondary objectives:

Secondary objectives were to determine the effect of Lactium® on:

- The evolution of the SBP due to an induced stress after a consumption of 2 weeks;
- The evolution of the diastolic blood pressure (DBP) and the heart rate due to an induced stress after a consumption of 2 and 6 weeks;
- The stress level after a consumption of 2 and 6 weeks;
- The evolution of salivary concentration of cortisol due to an induced stress after a consumption of 2 and 6 weeks (on a sub-population of 25 subjects per group);
- The global satisfaction of the subjects after 6 weeks of consumption.

3 Description of the study

3.1 Overall study design and plan - description

The study was a randomised, double-blind, parallel-group, placebo-controlled study.

Fifty-five subjects consumed Lactium® at dose 300 mg/day (Lactium® 300mg group) and 53 subjects consumed the placebo (placebo group).

The study products were consumed during 6 weeks.

Each subject came to BIOFORTIS for 4 visits:

- V0: pre-inclusion visit;
- V1: inclusion and experimental visit;
- V2: follow-up and experimental visit (2 weeks after V1);
- V3: experimental and end-of-study visit (6 weeks after V1).

Subjects interested in taking part in the study had to contact BIOFORTIS. They answered some preliminary questions including inclusion criteria. If they matched selection criteria, an appointment was scheduled for the 1st visit at BIOFORTIS.

V0: Pre-inclusion visit

When he arrived to BIOFORTIS, the volunteer read the information letter and if he agreed to take part in the study, he signed an informed consent.

The volunteer then filled in the HAD questionnaire to estimate his anxiety and depression level.

Next, the investigator should:

- Allocate an identification number (NS) to the subject in the chronological order;
- Conduct a clinical examination;
- Collect demographic data including date of birth, sex, height, weight and ethnic group;

- Collect medical history and the associate pathology;
- Collect possible concomitant medication;
- Check inclusion and non inclusion criteria.

Next, the clinical research technician/associate (CRT/CRA) gave some general instructions to the subject:

- Don't modify your usual physical activity during the study;
- Don't modify your dietary habits during the study (and no hypocaloric diet);
- Don't consume dietary supplements during the study;
- Don't modify your treatment during this study in the case your treatment is not forbidden during the study;
- Don't start a new treatment except extreme necessity.

And some instructions for the day before and the day of the visits:

- Come to BIOFORTIS with the same vehicle;
- Don't eat or drink half an hour before the visits;
- Eat your last meal at the same time before each visit;
- Go to bed at the same time in the evening before each visit;
- Don't do sport the day of the visit before to come to BIOFORTIS.

V1: Inclusion and experimental visit

The sequence of events was the following one:

1) The investigator checked that the instructions have been entirely respected since the last visit.

2) All the subjects realized a salivary sampling.

3) The psychologist explained the Stroop test to the subject in details to limit the bias of the stress due to the unknown.

4) The subject was in the test room and the armband to measure blood pressure was fit. A period of relaxation (R) of 6 minutes was respected. During the four last minutes, blood pressure and heart rate was measured every minute (R3, R4, R5 and R6). R6 corresponded to the beginning of the induced stress.

5) At R6, the test of induced stress was implemented and applied during 5 minutes (S) under control of the psychologist. Blood pressure and heart rate was measured every minute during the test (S1 to S5). The performance of the subject at the test was registered.

6) After this period, there was a relaxation period (P) of 6 minutes. At the third and the sixth minutes, blood pressure and heart rate were measured (P3 and P6).

7) All the subjects realized a salivary sampling 20 minutes after the end of the Stroop test.

8) Next, the investigator should:

- Conduct a clinical examination;
- Collect possible concomitant medication;
- Collect possible adverse events.

9) Next, the psychologist had the subject do the STAI questionnaire to evaluate the chronic stress.

Next, the CRA/CRT should:

- Randomize the subject;
- Give the product which corresponds to the randomization number (NR) to the subject in sufficient quantity for 2 weeks and ask him to bring the empty (or not) pill-box back at the next visit;
- Remind him the instructions he has to follow during the study.

V2: Follow-up and experimental visit (V1 + 2 weeks)

The sequence of events was the following one:

1) The investigator checked that the instructions have been entirely respected since the last visit.

2) Subjects of the cortisol group realized a salivary sampling.

3) The subject was in the test room and the armband to measure blood pressure was installed. A period of relaxation of 5 minutes was respected. During the four last minutes, blood pressure and heart rate was measured every minute (R3, R4, R5 and R6). R6 corresponded to the beginning of the induced stress.

4) At R6, the test of induced stress was implemented and applied during 5 minutes under control of the psychologist. Blood pressure and heart rate was measured every minute during the test (S1 to S5). The performance of the subject at the test registered.

5) After this period, there a relaxation period of 6 minutes. During the third and the sixth minutes, blood pressure and heart rate were measured (P3 and P6).

6) Subjects of the cortisol group realized a salivary sampling 20 minutes after the Stroop test (with the investigator).

7) Next, the investigator should:

- Conduct a clinical examination;
- Collect possible concomitant medication;
- Collect possible adverse events,

8) Next, the psychologist had the subject do the STAI questionnaire to evaluate the chronic stress.

Next, the CRA/CRT should:

- Get the pill-box back;
- Give the product which corresponds to the randomization number (NR) to the subject in sufficient quantity for 4 weeks;
- Remind him the instructions he had to follow during the study.

V3: Experimental and en-of-study visit (V1 + 6 weeks)

The sequence of events was the following one:

1) The investigator checked that the instructions have been entirely respected since the last visit.

2) Subjects of the cortisol group realized a salivary sampling.

3) The subject was in the test room and the armband to measure blood pressure was installed. A period of relaxation of 5 minutes was respected. During the four last minutes, blood pressure and heart rate were measured every minute (R3, R4, R5 and R6). R6 corresponded to the beginning of the induced stress.

4) At R6, the test of induced stress was implemented and applied during 5 minutes under control of the psychologist. Blood pressure and heart rate were measured every minute during the test (S1 to S5). The performance of the subject at the test was registered.

5) After this period, there was a relaxation period of 6 minutes. During the third and the sixth minutes, blood pressure and heart rate were measured (P3 and P6).

6) Subjects of the cortisol group realized a salivary sampling 20 minutes after the Stroop test.

7) Next, the investigator should:

- Conduct a clinical examination;
- Collect possible concomitant medication;
- Collect possible adverse events,

8) Next, the psychologist had the subject do the STAI questionnaire to evaluate the chronic stress.

Before leaving BIOFORTIS, the subject filled in a questionnaire of global satisfaction.

The modality of end-of study was explained to the subject.

3.2 Selection of study population

3.2.1 Inclusion criteria

To be included in the protocol, the subjects had to fulfil the following criteria:

- Healthy male and female subjects (representative of the European general population);
- Aged from 18 to 65 years old (limits included);
- With a Body Mass Index (BMI) between 18 and 27 kg/m² (limits included) (a tolerance of ± 2% was accepted in agreement with the promoter and the investigator but considered as a deviation);
- Non smoker or smoker up to 10 cigarettes per day (limits included);
- Blood pressure lower or equal to 140/90 mmHg;
- Heart rate between 50 and 100 bpm;
- With a HAD-A score lower or equal to 12 and a HAD-D score lower or equal to 8;
- Non-menopausal female subjects with reliable contraception for two cycles before the beginning of the study and agreeing to keep it during the entire duration of the study;
- Menopausal female subjects without hormone replacement therapy (HRT) or with HRT initiated at least two months before the beginning of the study and agreeing to keep it during the study;
- Agreeing not to modify their nutritional habits and their physical activity for the entire duration of the study;
- Capable and willing to conform to the protocol and accepting to give his written informed consent;
- Registered to Social Security regimen;
- Accepting to be registered with the Volunteers in biomedical research file.

3.2.2 Non-inclusion criteria

Subjects with the following criteria could not be included in the protocol:

- Known allergy to one of the tested products' components or to related products;
- Neurologic or psychiatric pathologies;

- Significant psychiatric troubles (in particular schizophrenic troubles, anxious and/or depressive major troubles, suicidal idea etc.);
- Pathologies which could interfere with the study in the investigator's opinion;
- Psychopharmacologic or neurologic treatments (anxiolytic, beta-blockers, antidepressant, anticonvulsant etc.);
- Intake of nutritional supplements (in case of consumption of nutritional supplements, a V0 would be done 4 weeks after the total stopping of the intake);
- Intake of antihypertensive drug;
- Treatments which could interfere with the study in the investigator's opinion;
- Drugs consumption;
- Alcohol consumption higher than 2 glasses per day, every day;
- Vacations during the study period;
- Planned stress period during the study period;
- Subject having already performed the Stroop test or the STAI questionnaire;
- Colour-blind subjects;
- Breastfeeding or pregnant woman or woman desiring to be pregnant in the following month;
- Having a particular diet (hypocaloric diet, intolerance to gluten, vegetarian diet, etc.) or presenting a history of food behavioural problem;
- Taking part in an-other clinical trial or being in the exclusion period of a previous clinical trial;
- Presenting a psychological or linguistic incapability to sign the informed consent;
- Refusing to sign the informed consent;
- Under legal protection (guardianship, wardship) or deprived from his rights following administrative or judicial decision;
- Having received, during the last 12 months, indemnities for clinical trial higher or equal to 4500 Euros;
- Impossible to contact in case of emergency.

3.3 Test products

3.3.1 Presentation of the products

The study products were presented as capsules packaged in pill-box of 35 capsules.

They should be stored at room temperature.

The subjects had to consume one capsule per day, in the evening, about one hour before sleeping, with a glass of water.

3.3.2 Details on test products

Lactium® 300mg

→ *Composition*

	Weight in mg/capsule
Milk protein hydrolysate	300.0
Maltodextrin	26.0
Magnesium stearate	5.0
Colloidal silica	2.0

→ *Lot number:* NM10 – 15001

→ *Use-by date:* 12/2011

Placebo

→ *Composition*

	Weight in mg/capsule
Maltodextrin	309.0
Magnesium stearate	5.0
Colloidal silica	2.0

→ *Lot number:* NM10 – 15001

→ *Use-by date:* 12/2011

3.3.3 Method of assigning products to subjects

Products were randomly allocated to the subjects, according to a table of randomization generated using the software SAS 9.1.3 Service Pack 4.The allocation of subjects to the groups was performed with an adaptative stratified randomisation. The covariables which were used to adapt the randomisation are the following factors:

- Gender with 2 levels: man and woman;
- Categorized variation of SBP during inducted stress (Δ), with 4 levels:
  - Level 1: $\Delta < 10$ mmHg;
  - Level 2: $10 \text{ mmHg} \leq \Delta < 20$ mmHg;
  - Level 3: $20 \text{ mmHg} \leq \Delta < 30$ mmHg;
  - Level 4: $30 \text{ mmHg} \leq \Delta$.

The minimisation method (Pocock & Simon, 1975) permits to randomize the subjects by minimising the possible imbalance between the numbers of subjects in each group over all the levels of our 2 factors.

The products were prepared and distributed by the CRA after inclusion of subject.

3.3.4 Blinding

Products were packaged in such a way that it was not possible to discriminate the different products.

3.4 Efficiency assessment

At V1, V2 and V3, blood pressure and heart rate were measured every minute of the test session using a blood pressure monitor. For each parameter (SBP, DBP and heart rate), five data were extrapolated from these measurements:

- The rest mean (mean of data picked out on the 4th (R4), the 5th (R5) and the 6th (R6) minute of resting period before induction of the stress);
- The S mean (mean of data picked out during the 5 minutes of the induced stress (S1 to S5));
- The S max (the higher data picked out during the induced stress);
- P3 and P6 (the data picked out respectively during the 3rd and the 6th minute of resting period after the induced stress).

For cortisol concentration analysis, the saliva was collected with a Salivette® before the Stroop test and 20 minutes after its completion. The cortisol concentration was determined by electrochemiluminescence (Elecsis).

During the Stroop test, two kinds of data were picked out:

- The number of words read;
- The number of mistakes (a mistake was counted when the subject failed twice on a word).

The STAI questionnaire was filled in by the subjects at V1 and V3, after the Stroop test.

The global satisfaction questionnaire was filled in by the subjects at V3.

Primary outcome

The primary parameter is the variation of SBP between the reference value for rest (mean of R4, R5 and R6) and the reference value for stress (mean of values S1 to S5) at V3.

Secondary outcomes

The secondary outcomes are:

- The variation of SBP, DBP and heart rate between value for rest (mean of R4, R5 and R6) and the maximal value during induced stress at V1, V2 and V3;
- The variation of SBP between the reference value for rest (mean of R4, R5 and R6) and the reference value for stress (mean of values S1 to S5) at V1 and V2;
- The variation of DBP and heart rate between the reference value for rest (mean of R4, R5 and R6) and the reference value for stress (mean of values S1 to S5) at V1, V2 and V3;
- The variation of the SBP, DBP and heart rate between value for rest (mean of R4, R5 and R6) and value after the induced stress (P3 and P6) at V1, V2 and V3;
- The variation of salivary cortisol concentration between before and after Stroop test at V1, V2 and V3;
- The score of STAI questionnaire at V1, V2 and V3;
- The Stroop test score (defined as the difference between the number of words named and the number of mistakes), the number of words named and the number of mistakes;
- The questionnaire of global satisfaction at V3.

3.5 Statistics

As there is very little missing data in population, only intergroup main analysis was used on ITT population with Expectation-Maximization replacement of data (by sex and product).

Missing data

As there is very little missing data in population no replacement was performed. The only replacement concerns the primary criteria on which an ITT intergroup analysis was performed. The Expectation-Maximization algorithm was used for this replacement of data made by product.

Statistical methods

Statistical analysis was performed by BIOFORTIS with the software SAS 9.1.3 Service Pack 4. The significance threshold associated with the study was of 5%.

General statistical elements

All data are listed by group and by subject.

The following descriptive statistics are provided by group and visit depending on the nature of variables:

- Quantitative variables: number of observed values, mean and standard deviation (SD), minimum (Min), median (Med) and maximum (Max);
- Qualitative variables: number of observed values, number and percentage by class.

Graphs of mean ± SEM are provided for quantitative variable. Bar charts or pie charts are provided for qualitative variable.

Population description

Description of all the volunteers, including the ones not included, the ones included who prematurely withdraw and the ones who finished the study, is provided with absolute (N) and relative (%) frequency. Premature withdrawal reasons are listed.

Descriptive statistics are used to describe volunteers at baseline.

Main analysis

The SBP change following an induced stress at V3 is analysed by the ANCOVA model after: Y_{v3} = Product + Sex + Y_{v1}

This analysis of covariance compares Lactium® 300mg group with the placebo.

Secondary analysis

Homogeneity at baseline (V1) of all quantitative variables is verified by the analysis of variance after: Y = Product + Sex

All quantitative variables at V2, V3 are analyzed as the primary criteria.

To complete intergroup analyses, intragroup analyses between V1 and V2/V3 are performed with paired Student's T test.

For each criterion studied during induced stress, statistic descriptive of variable on rest, on stress, of their variation (stress-rest) and of variable on recovery are presented.

For the questionnaire of global satisfaction, items on the product efficiency and tolerance are analyzed with a Wilcoxon-Mann-Witney test and items on satisfaction are analyzed with a Chi-2 test.

Note: For the analysis of cortisol the factor 'moment of the day' (before 12:00 or after 11:59) was used as factor of adjustment in all analysis.

4 Results

The data detailed in this report come from the statistical analysis on PP population, which is equivalent to ITT population.

Statistical significance is expressed as following:

* (significant): $p < 0.05$;

** (significant): $p < 0.01$;

*** (significant): $p < 0.001$.

4.1 Hemodynamic parameters

4.1.1 Systolic blood pressure

The descriptive statistics of SBP raw data during the test sessions are presented in the following table. The variations from V1 are illustrated in figure 1.

The descriptive statistics of SBP, during and after induced stress and expressed as variations from SBP at rest are presented in the table 2. The variations from V1 are illustrated in figures 2 to 4.

The data are expressed in mmHg.

Table 1: *SBP during the test sessions*

Visit	Variable	Placebo (N=52)	Lactium® 300mg (N=55)	Intergroup p#
V1	Rest	113.6 ± 11.9	111.2 ± 12.0	0.2622
	Average stress	132.2 ± 16.0	130.2 ± 17.8	
	Maximum stress	141.5 ± 18.6	138.9 ± 20.2	
	P3	110.9 ± 11.9	109.6 ± 11.4	
	P6	108.4 ± 13.6	108.2 ± 10.5	
V2	Rest	109.9 ± 12.2	108.5 ± 12.8	0.6696
	Average stress	126.5 ± 15.8	125.4 ± 19.1	
	Maximum stress	135.3 ± 17.5	133.8 ± 20.2	
	P3	106.9 ± 12.7	106.3 ± 13.2	
	P6	106.7 ± 10.9	104.3 ± 12.2	
V3	Rest	110.6 ± 11.0	109.0 ± 13.5	0.8432
	Average stress	126.3 ± 15.2	124.2 ± 18.1	
	Maximum stress	134.5 ± 17.2	131.5 ± 19.8	
	P3	109.4 ± 10.9	107.2 ± 12.4	
	P6	108.0 ± 11.6	105.5 ± 11.2	

 # ANOVA (Product Sex) at V1 and ANCOVA (Product Sex Baseline) at V2, V3

Intergroup analysis shows no significant intergroup difference at baseline (V1) and no product effect at V2 and V3 on SBP at rest.

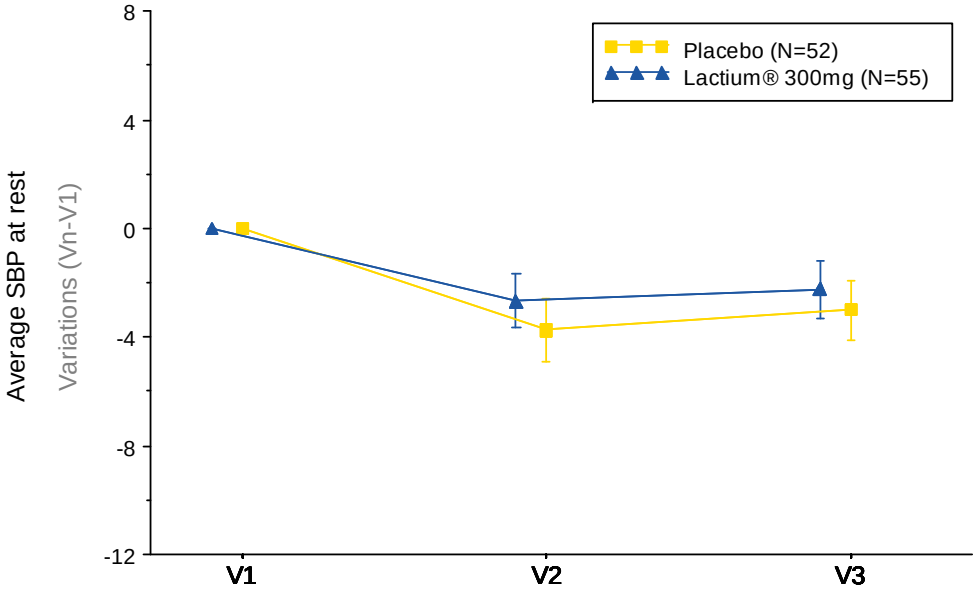

Figure 1: **Evolution of SBP at rest (variation from V1)**

Table 2: *SBP during the test sessions, expressed as a variation of SBP rest mean*

Visit	Variable	Placebo (N=52)	Lactium® 300mg (N=55)	Intergroup p#
V1	Average stress - Rest	18.6 ± 8.9	19.0 ± 9.5	0.8289
	Maximum stress - Rest	27.8 ± 11.5	27.6 ± 12.1	0.9270
	P3 - Rest	-2.7 ± 5.7	-1.6 ± 4.8	0.3115
	P6 - Rest	-5.2 ± 6.8	-3.0 ± 5.8	0.0749
V2	Average stress - Rest	16.6 ± 8.8	16.9 ± 11.8	0.9722
	Maximum stress - Rest	25.5 ± 11.4	25.3 ± 13.2	0.9781
	P3 - Rest	-3.0 ± 5.6	-2.2 ± 6.4	0.6847
	P6 - Rest	-3.2 ± 5.5	-4.3 ± 7.0	0.2310
V3	Average stress - Rest	15.7 ± 8.3	15.2 ± 10.3	0.5726
	Maximum stress - Rest	23.8 ± 10.4	22.5 ± 11.8	0.4615
	P3 - Rest	-1.3 ± 7.0	-1.7 ± 6.2	0.5444
	P6 - Rest	-2.7 ± 6.1	-3.5 ± 6.5	0.3233

 # ANOVA (Product Sex) at V1 and ANCOVA (Product Sex Baseline) at V2, V3

Intergroup analysis shows no reactivity of SBP to induced stress.

Table 3: *Intragroup analysis of SBP 'S mean - rest mean'*

Comparison	Product	N	DF	Test value	P value	Difference [95% CI]
V2 - V1	Placebo	52	51	-1.89	0.0647	-2.0 [-4.1;0.1]
	Lactium® 300mg	55	54	-2.23	0.0299 (*)	-2.1 [-4.0;-0.2]
V3 - V1	Placebo	52	51	-2.71	0.0092 (**)	-2.9 [-5.0;-0.7]
	Lactium® 300mg	55	54	-4.00	0.0002 (***)	-3.7 [-5.6;-1.9]

Intragroup analysis highlights that the absence of reactivity to induced stress is linked to a significant positive evolution of SBP 'S mean - rest mean' between V3 and V1 in the two groups. The decrease in SBP 'S mean - rest mean' is observed with significativity in the Lactium® 300 mg group at V2, compared with V1 (p=0.0299; diff=-2.1 mmHg), and as a trend in the placebo group.

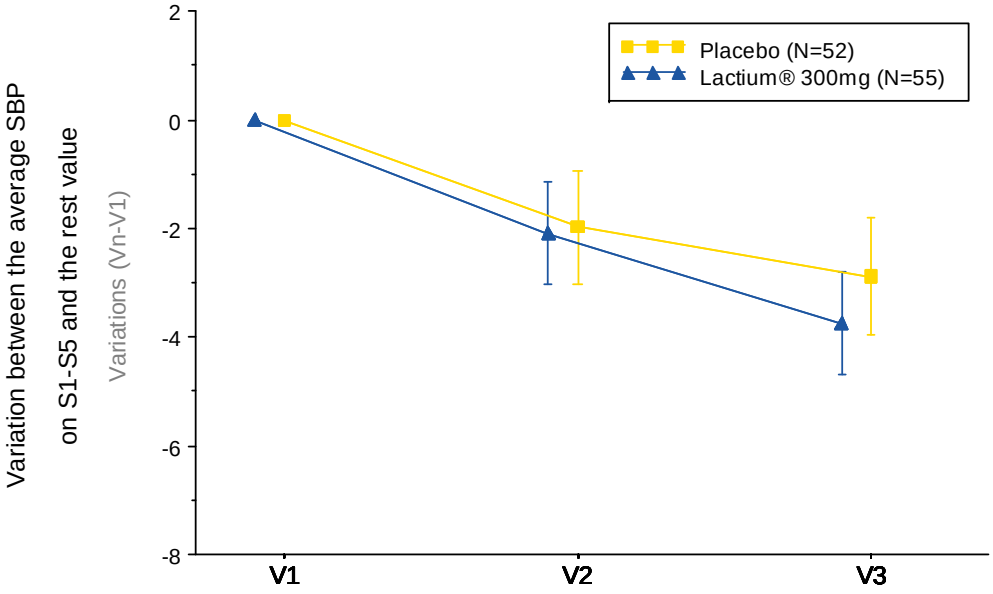

Figure 2: **Evolution of SBP 'S mean - rest mean' (variation from V1)**

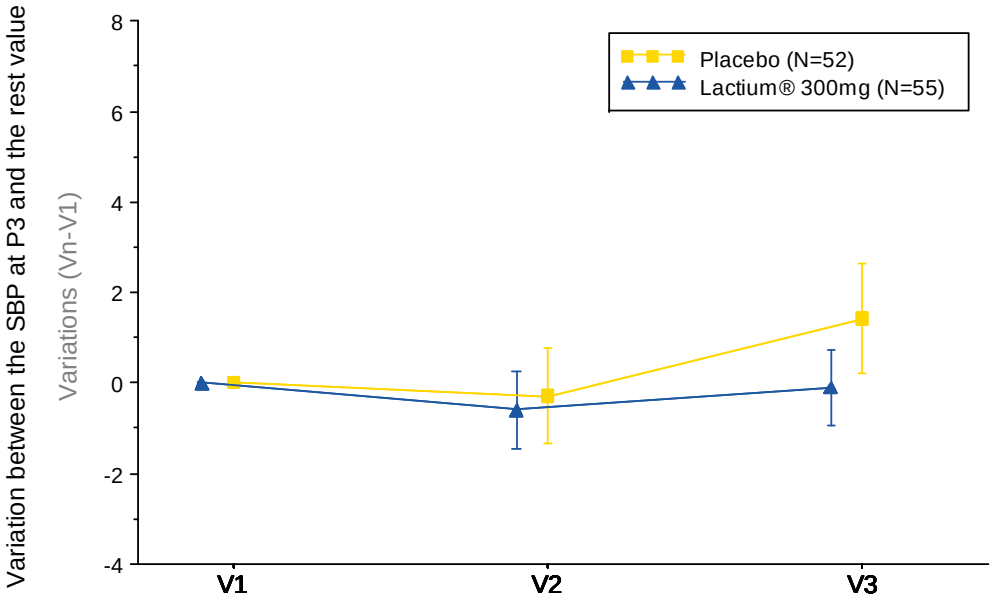

Figure 3: **Evolution of SBP 'P3 - rest mean' (variation from V1)**

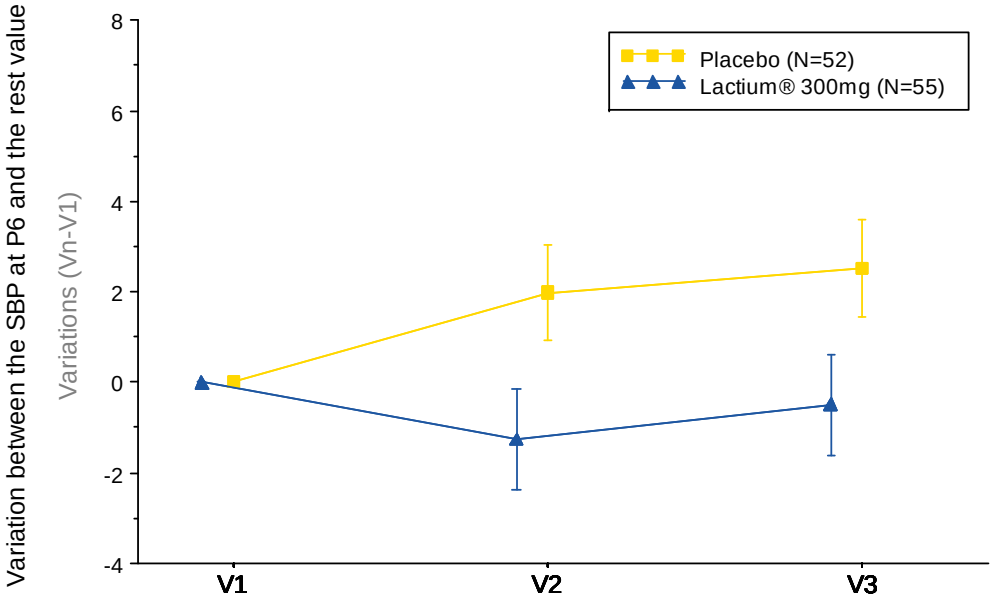

Figure 4: **Evolution of SBP 'P6 - rest mean' (variation from V1)**

4.1.2 Diastolic blood pressure

The descriptive statistics of DBP raw data during the test sessions are presented in the following table. The variations from V1 are illustrated in figure 5.

The descriptive statistics of DBP, during and after induced stress and expressed as variations from DBP at rest are presented in the table 5. The variations from V1 are illustrated in figures 6 to 8.

The data are expressed in mmHg.

Table 4: *DBP during the test sessions*

Visit	Variable	Placebo (N=52)	Lactium® 300mg (N=55)	Intergroup p#
V1	Rest	67.2 ± 7.8	64.6 ± 7.9	0.0773
	Average stress	75.3 ± 8.7	74.2 ± 8.4	
	Maximum stress	80.3 ± 9.4	79.6 ± 10.0	
	P3	62.8 ± 8.8	61.0 ± 7.4	
	P6	60.5 ± 9.6	59.1 ± 7.8	
V2	Rest	66.8 ± 8.2	63.8 ± 6.9	0.2839
	Average stress	73.8 ± 8.4	71.9 ± 7.6	
	Maximum stress	78.8 ± 9.1	76.3 ± 8.1	
	P3	62.6 ± 8.6	59.9 ± 6.8	
	P6	61.9 ± 8.5	59.6 ± 6.9	
V3	Rest	67.4 ± 8.3	64.0 ± 7.7	0.1596
	Average stress	73.7 ± 8.7	71.7 ± 8.7	
	Maximum stress	78.1 ± 9.6	76.3 ± 9.4	
	P3	63.8 ± 9.2	59.8 ± 8.0	
	P6	63.2 ± 9.0	59.8 ± 7.8	

 # ANOVA (Product Sex) at V1 and ANCOVA (Product Sex Baseline) at V2, V3

Intergroup analysis shows no significant intergroup difference at baseline (V1) and no product effect at V2 and V3 on DBP at rest.

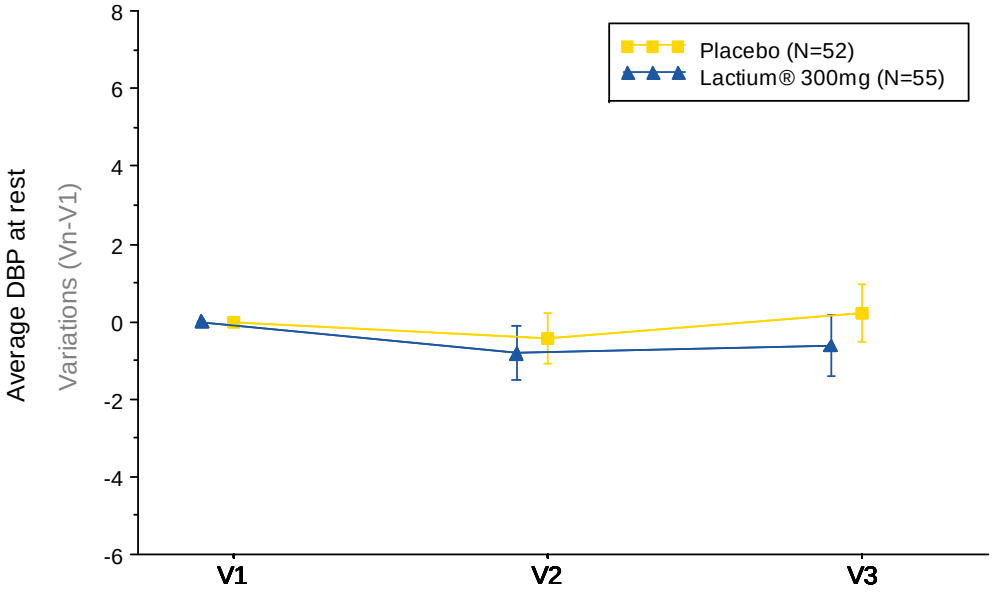

Figure 5: **Evolution of DBP at rest (variation from V1)**

Table 5: *DBP during the test sessions, expressed as a variation of DBP rest mean*

Visit	Variable	Placebo (N=52)	Lactium® 300mg (N=55)	Intergroup p#
V1	Average stress - Rest	8.1 ± 4.4	9.6 ± 4.6	0.0703
	Maximum stress - Rest	13.1 ± 4.7	15.0 ± 5.3	0.0559
	P3 - Rest	-4.3 ± 5.2	-3.6 ± 5.8	0.4596
	P6 - Rest	-6.7 ± 5.7	-5.5 ± 5.8	0.2575
V2	Average stress - Rest	7.0 ± 4.4	8.1 ± 5.2	0.9274
	Maximum stress - Rest	12.0 ± 5.1	12.5 ± 5.6	0.5707
	P3 - Rest	-4.2 ± 4.1	-3.9 ± 5.1	0.9344
	P6 - Rest	-4.9 ± 5.2	-4.2 ± 5.8	0.9547
V3	Average stress - Rest	6.3 ± 4.7	7.7 ± 4.5	0.4561
	Maximum stress - Rest	10.7 ± 4.7	12.3 ± 4.9	0.3824
	P3 - Rest	-3.6 ± 6.0	-4.2 ± 5.2	0.4035
	P6 - Rest	-4.3 ± 5.4	-4.2 ± 5.7	0.5696

 # ANOVA (Product Sex) at V1 and ANCOVA (Product Sex Baseline) at V2, V3

Intergroup analysis shows no reactivity of DBP to induced stress, whatever the product consumed.

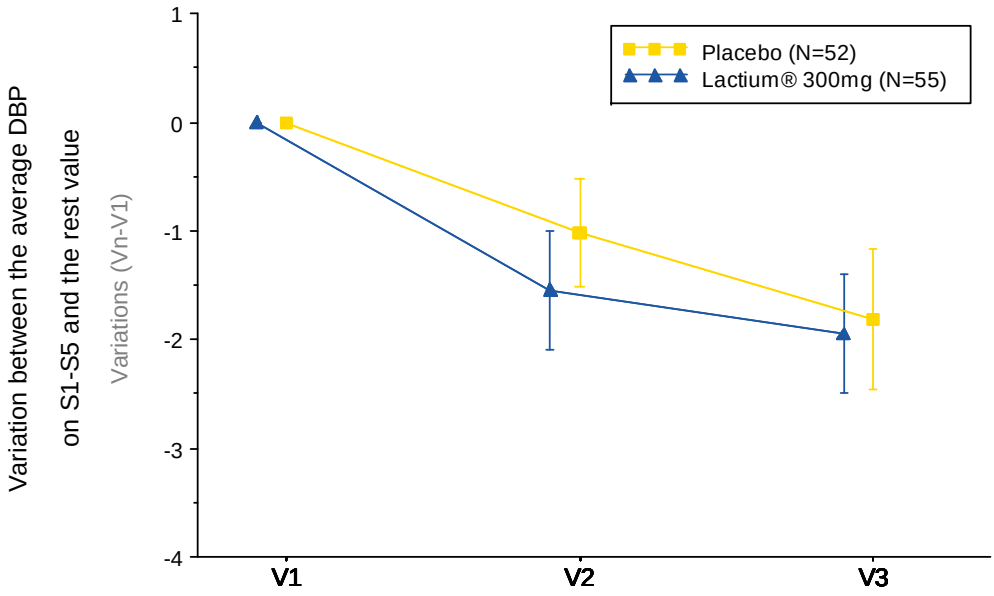

Figure 6: **Evolution of DBP 'S mean - rest mean' (variation from V1)**

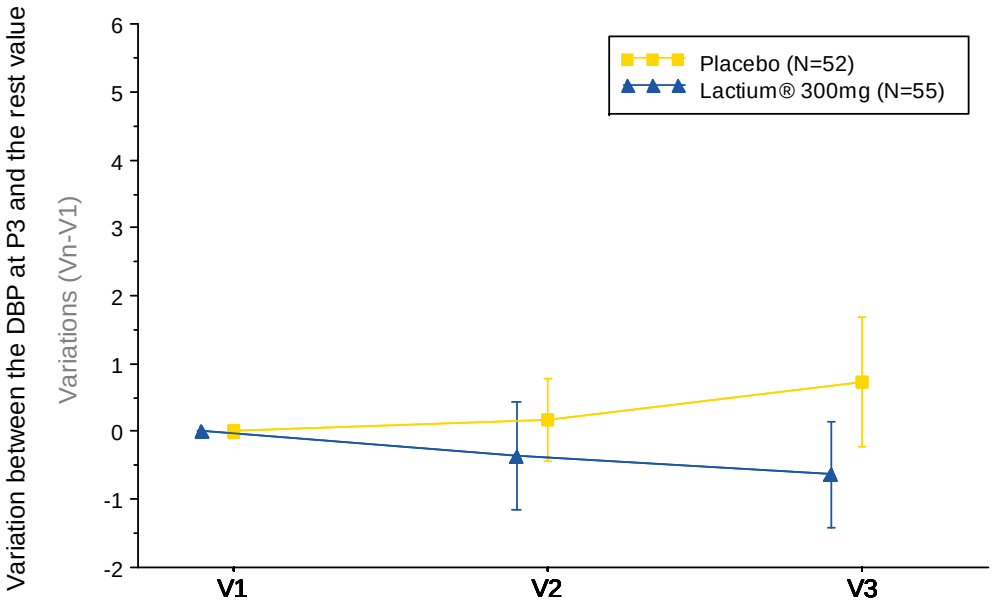

Figure 7: **Evolution of DBP 'P3 - rest mean' (variation from V1)**

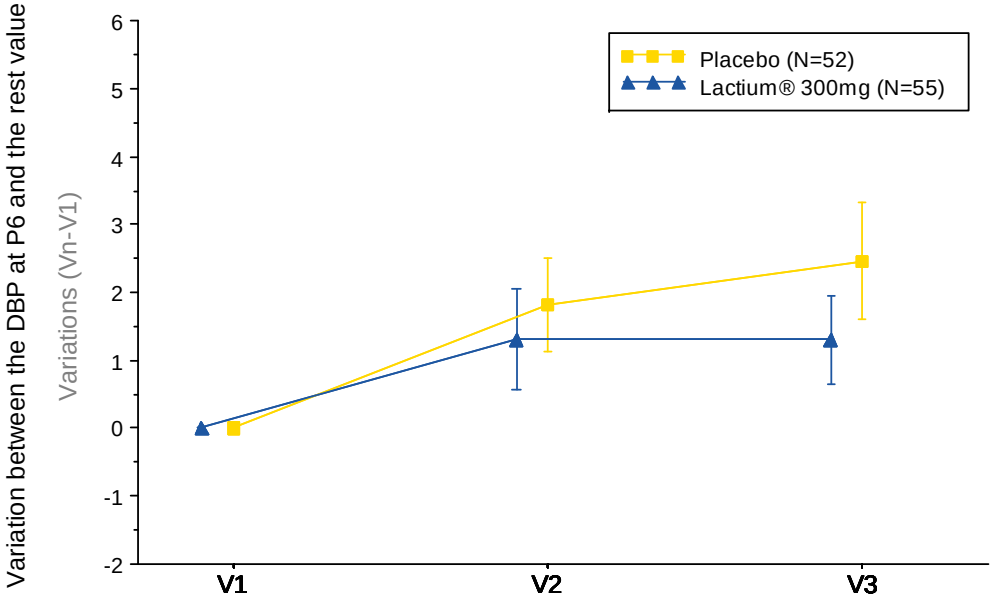

Figure 8: **Evolution of DBP 'P6 - rest mean' (variation from V1)**

4.1.3 Heart rate

The descriptive statistics of heart rate raw data during the test sessions are presented in the following table. The variations from V1 are illustrated in figure 9.

The descriptive statistics of heart rate, during and after induced stress and expressed as variations from heart rate at rest are presented in the table 7. The variations from V1 are illustrated in figures 10 to 12.

The data are expressed in bpm.

Table 6: Heart rate during the test sessions

Visit	Variable	Placebo (N=52)	Lactium® 150mg (N=53)	Lactium® 300mg (N=55)	Intergroup p#
V1	Rest	75.7 ± 9.1	78.6 ± 12.1	76.4 ± 15.7	0.7572
	Average stress	87.3 ± 12.8	91.0 ± 13.6	90.1 ± 17.9	
	Maximum stress	94.2 ± 14.4	98.8 ± 14.9	97.9 ± 19.0	
	P3	73.0 ± 9.3	74.7 ± 10.9	73.8 ± 15.5	
	P6	72.0 ± 9.5	73.9 ± 10.9	72.6 ± 14.8	
V2	Rest	76.5 ± 10.2	78.2 ± 11.1	78.4 ± 15.2	0.2965
	Average stress	86.0 ± 12.4	88.6 ± 12.7	87.3 ± 17.1	
	Maximum stress	92.2 ± 14.4	95.0 ± 15.7	94.9 ± 19.2	
	P3	74.0 ± 9.7	74.2 ± 10.9	73.0 ± 13.1	
	P6	72.6 ± 10.0	73.3 ± 10.5	72.3 ± 13.2	
V3	Rest	75.3 ± 10.1	77.3 ± 14.7	76.2 ± 13.9	0.7829
	Average stress	83.4 ± 11.8	87.8 ± 15.1	85.2 ± 16.4	
	Maximum stress	88.8 ± 14.4	93.8 ± 16.6	91.4 ± 18.1	
	P3	72.7 ± 10.2	72.9 ± 12.4	71.7 ± 12.3	
	P6	70.9 ± 9.7	72.1 ± 12.0	70.3 ± 11.8	

 # ANOVA (Product Sex) at V1 and ANCOVA (Product Sex Baseline) at V2, V3

Intergroup analysis shows no significant intergroup difference at baseline (V1) and no product effect at V2 and V3 on heart rate at rest.

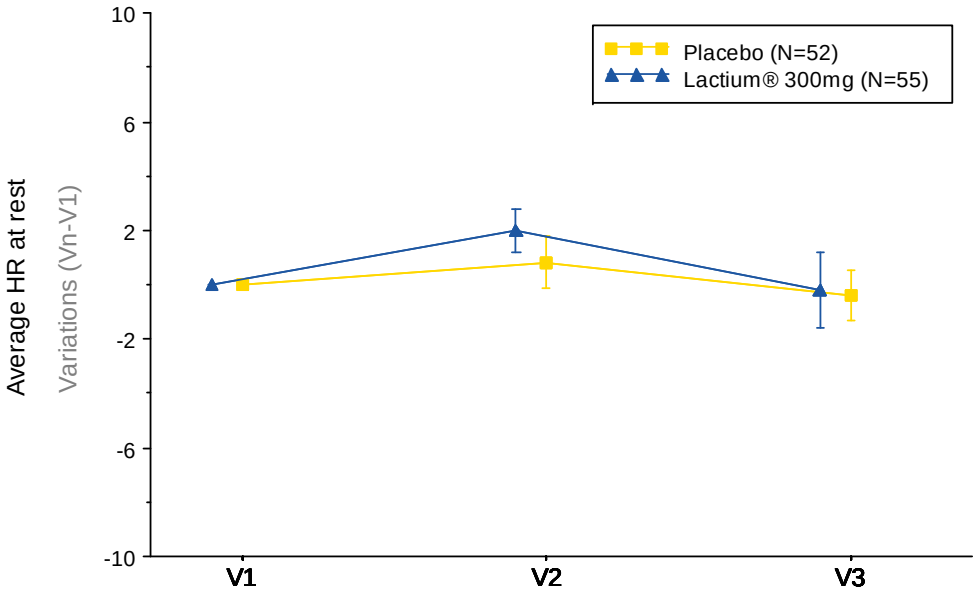

Figure 9: **Evolution of heart rate at rest (variation from V1)**

Table 7: Heart rate during the test sessions, expressed as a variation of heart rate rest mean

Visit	Variable	Placebo (N=52)	Lactium® 300mg (N=55)	Intergroup p#
V1	Average stress - Rest	11.6 ± 8.3	13.6 ± 9.8	0.2447
	Maximum stress - Rest	18.5 ± 10.7	21.4 ± 12.4	0.1945
	P3 - Rest	-2.7 ± 4.5	-2.6 ± 5.9	0.9405
	P6 - Rest	-3.7 ± 4.8	-3.9 ± 5.7	0.8318
V2	Average stress - Rest	9.5 ± 7.3	8.8 ± 6.9	0.0806
	Maximum stress - Rest	15.7 ± 9.9	16.4 ± 10.5	0.4630
	P3 - Rest	-2.5 ± 4.3	-5.5 ± 7.2	0.0041 (**)
	P6 - Rest	-3.9 ± 4.5	-6.1 ± 7.3	0.0399 (*)
V3	Average stress - Rest	8.1 ± 7.1	9.0 ± 6.8	0.9525
	Maximum stress - Rest	13.5 ± 10.0	15.2 ± 9.5	0.9639
	P3 - Rest	-2.6 ± 4.5	-4.5 ± 7.7	0.0800
	P6 - Rest	-4.3 ± 4.5	-5.9 ± 7.4	0.1996

 # ANOVA (Product Sex) at V1 and ANCOVA (Product Sex Baseline) at V2, V3

Intergroup analysis shows no reactivity of heart rate to induced stress (average and maximum value), whatever the product consumed. However, at V2, a significant product effect is observed on heart rate ‘P3 - rest’ (p=0.0041) and ‘P6 - rest’ (p=0.0399). This product effect is related to a significant decrease in heart rate ‘P3 - rest’ and heart rate ‘P6 - rest’ under Lactium® 300 mg compared with placebo (V2: diff=-3.0 bpm; V3: diff=-2.0 bpm). The recovery of heart rate after induced stress is so better in Lactium® 300 mg group than in placebo group.

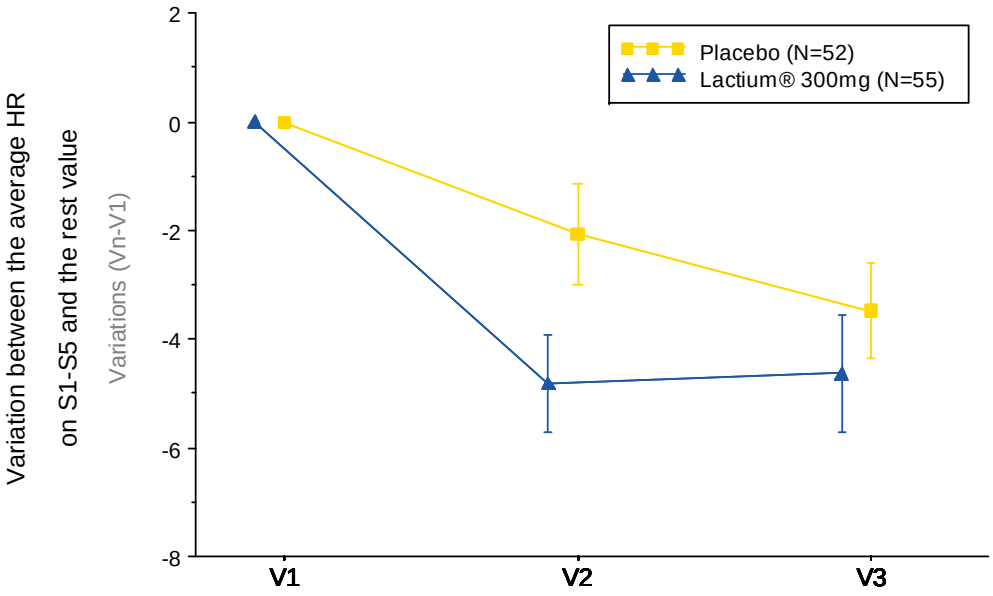

Figure 10: **Evolution of heart rate 'S mean - rest mean' (variation from V1)**

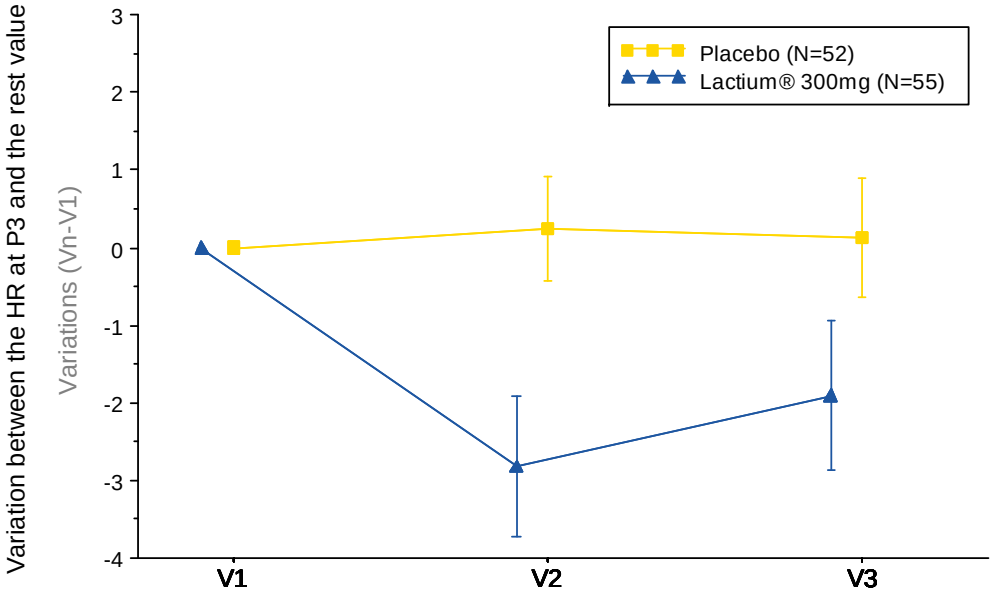

Figure 11: **Evolution of heart rate 'P3 - rest mean' (variation from V1)**

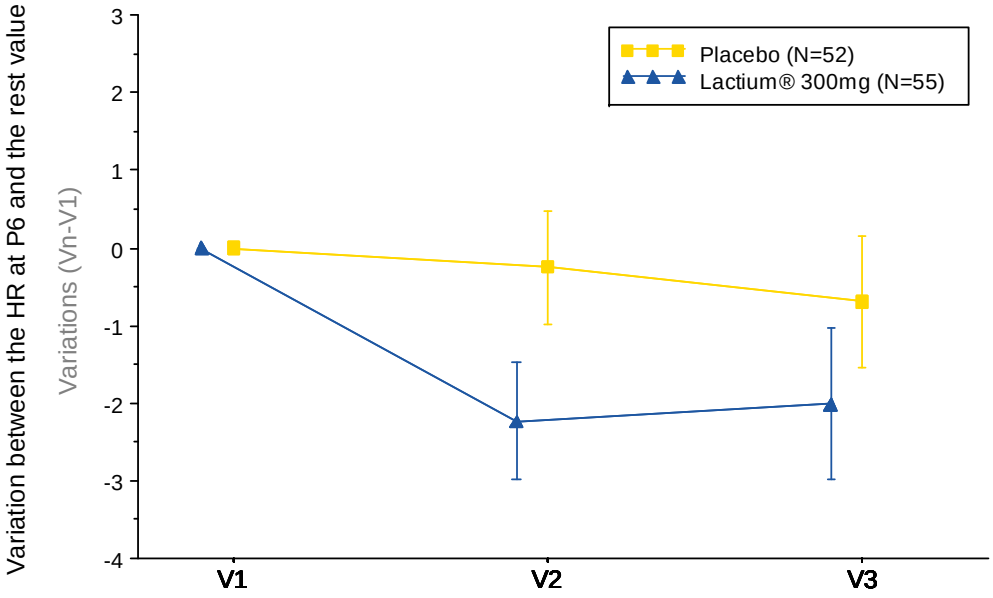

Figure 12: **Evolution of heart rate 'P6 - rest mean' (variation from V1)**

4.2 Cortisol

The descriptive statistics of salivary cortisol concentration raw data during the test sessions, as well as variation of salivary cortisol concentration before and after the test session are presented in the following tables. The data are illustrated in figures 13 and 14.

The data are expressed in nmol/L.

Table 8: *Salivary cortisol concentration during the test sessions*

Visit	Variable	Placebo (N=25)	Lactium® 300mg (V1=25, V2=24, V3=25)	Intergroup p#
V1	Before induced stress	10.07 ± 6.23	10.43 ± 7.11	
	After induced stress	10.11 ± 6.39	10.71 ± 7.03	
	Variation after-before induced stress	0.04 ± 4.64	0.28 ± 5.36	0.8823
V2	Before induced stress	10.23 ± 4.85	12.07 ± 7.07	
	After induced stress	9.36 ± 5.41	11.29 ± 6.20	
	Variation after-before induced stress	-0.87 ± 4.03	-0.74 ± 2.89	0.9361
V3	Before induced stress	10.88 ± 4.83	12.92 ± 10.01	
	After induced stress	8.42 ± 4.46	10.58 ± 7.55	
	Variation after-before induced stress	-2.46 ± 3.34	-2.53 ± 3.26	0.6264

 # ANOVA (Product Sex Moment) at V1 and ANCOVA (Product Sex Moment Baseline) at V2, V3

Intergroup analysis shows no reactivity of cortisol salivary to induced stress, whatever the product consumed.

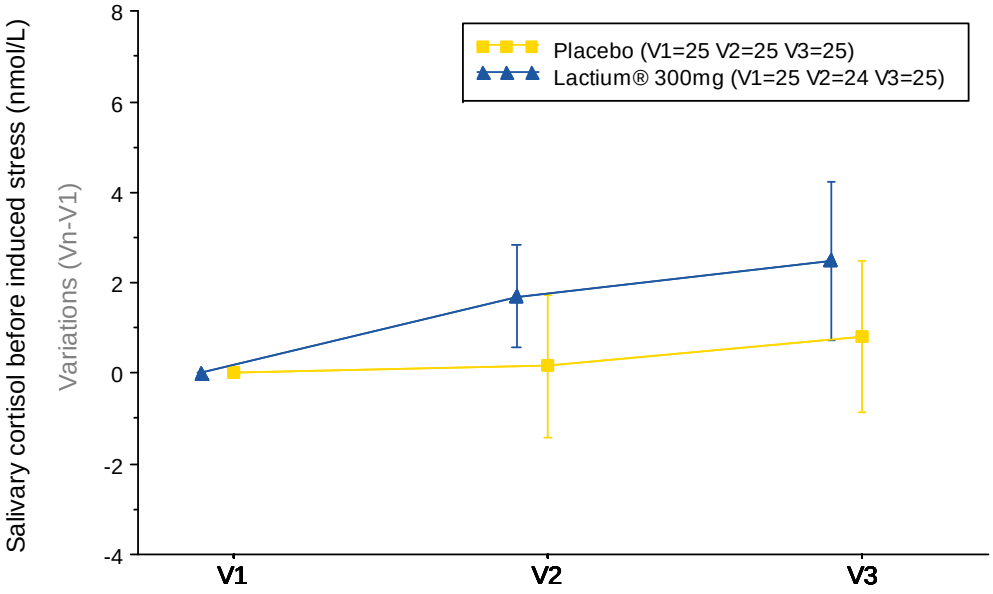

Figure 13: **Evolution of salivary cortisol concentration before stress (variation from V1)**

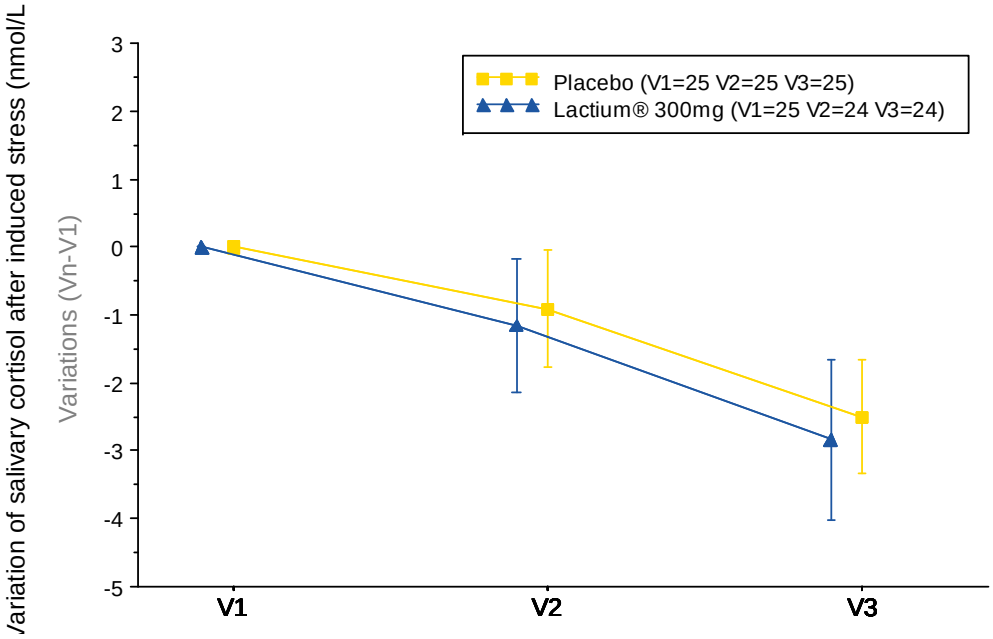

Figure 14: **Evolution of salivary cortisol concentration 'before - after stress' (variation from V1)**

4.3 Stroop test

4.3.1 Stroop test score

The descriptive statistics of the Stroop test score are presented in the following table and illustrated in figure 15. The data are expressed in arbitrary units (a.u).

Table 9: Stroop test score

Visit	Statistics	Placebo (N=52)	Lactium® 300mg (N=55)	Intergroup p#
V1	Mean±SD	279.8 ± 56.9	280.0 ± 53.5	0.9902
	(Min;Max)	(150 ; 414)	(163 ; 444)	
V2	Mean±SD	325.6 ± 64.0	332.2 ± 64.5	0.2170
	(Min;Max)	(177 ; 497)	(212 ; 534)	
V3	Mean±SD	342.2 ± 68.4	349.9 ± 63.1	0.2012
	(Min;Max)	(200 ; 518)	(216 ; 549)	

 # ANOVA (Product Sex) at V1 and ANCOVA (Product Sex Baseline) at V2, V3

Intergroup analysis shows no significant intergroup difference at baseline (V1) and no product effect at V2 and V3 on Stroop test score.

However, intragroup analysis reveals a significant increase in Stroop test score in each group, at V2 and V3 compared with V1.

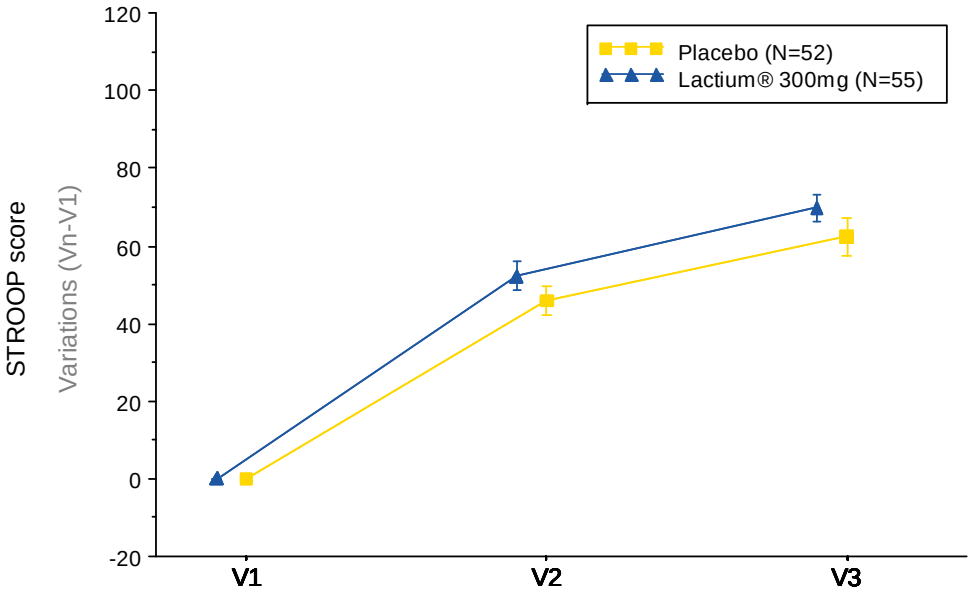

Figure 15: **Evolution of the Stroop test score (variation from V1)**

4.3.2 Number of words named

The descriptive statistics of the number of words named during the Stroop test are presented in the following table and illustrated in figure 16.

Table 10: *Number of words named*

Visit	Statistics	Placebo (N=52)	Lactium® 300mg (N=55)	Intergroup p#
V1	Mean±SD	283.4 ± 56.0	283.9 ± 52.9	0.9620
	(Min;Max)	(161 ; 415)	(167 ; 445)	
V2	Mean±SD	328.5 ± 63.0	335.7 ± 63.9	0.1945
	(Min;Max)	(178 ; 497)	(219 ; 534)	
V3	Mean±SD	344.8 ± 67.8	353.2 ± 62.6	0.1720
	(Min;Max)	(202 ; 518)	(224 ; 549)	

 # ANOVA (Product Sex) at V1 and ANCOVA (Product Sex Baseline) at V2, V3

Intergroup analysis shows no significant intergroup difference at baseline (V1) and no product effect at V2 and V3 on the number of words names during the Stroop test.

Once again, intragroup analysis reveals a significant increase in the number of words named in each group, at V2 and V3 compared with V1.

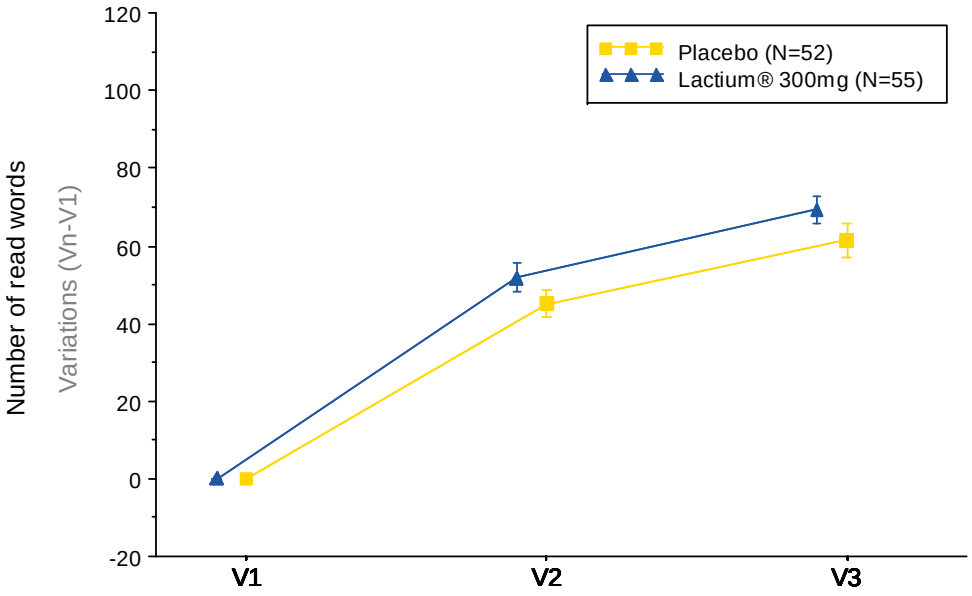

Figure 16: **Evolution of the number of words named during the Stroop test (variation from V1)**

4.3.3 Number of mistakes

The descriptive statistics of the number of mistakes during the Stroop test are presented in the following table and illustrated in figure 20.

Table 11: Number of mistakes

Visit	Statistics	Placebo (N=52)	Lactium® 300mg (N=55)	Intergroup p#
V1	Mean±SD	3.5 ± 2.9	3.9 ± 3.4	0.5506
	(Min;Max)	(0 ; 11)	(0 ; 12)	
V2	Mean±SD	2.9 ± 3.2	3.5 ± 3.1	0.5300
	(Min;Max)	(0 ; 15)	(0 ; 12)	
V3	Mean±SD	2.6 ± 2.9	3.3 ± 3.0	0.2085
	(Min;Max)	(0 ; 14)	(0 ; 13)	

 # ANOVA (Product Sex) at V1 and ANCOVA (Product Sex Baseline) at V2, V3

Intergroup analysis shows no significant intergroup difference at baseline (V1) and no product effect at V2 and V3 on the number of mistakes during the Stroop test.

Intragroup analysis reveals a significant decrease in the number of mistakes in the placebo group at V3 compared with V1 (p=0.0086; diff=-1.0) and a trend in Lactium® 300 mg group (p=0.0816, diff=-0.6).

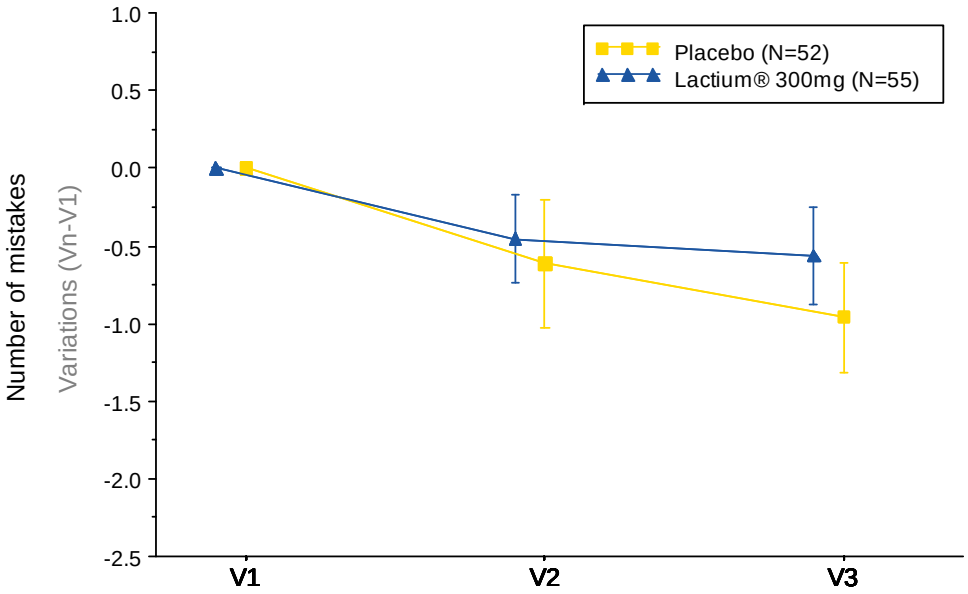

Figure 17: **Evolution of the number of mistakes during the Stroop test (variation from V1)**

4.4 STAI questionnaire

The descriptive statistics of STAI questionnaire score are presented in the following table and illustrated in figure 18. The data are expressed in a.u.

Table 12: *STAI questionnaire score*

Visit	Statistics	Placebo (N=52)	Lactium® 300mg (N=55)	Intergroup p#
V1	Mean±SD	28.7 ± 5.7	31.2 ± 7.6	0.0518
	(Min;Max)	(20 ; 47)	(20 ; 48)	
V2	Mean±SD	28.4 ± 7.5	27.7 ± 6.1	0.0143 (*)
	(Min;Max)	(20 ; 48)	(20 ; 51)	
V3	Mean±SD	26.5 ± 6.3	26.6 ± 5.5	0.1012
	(Min;Max)	(20 ; 54)	(20 ; 39)	

 # ANOVA (Product Sex) at V1 and ANCOVA (Product Sex Baseline) at V2, V3

Intergroup analysis shows no significant intergroup difference at baseline (V1)

A significant product effect is observed at V2 (p=0.0143). This effect product is related to a decrease in STAI score in Lactium® 300 mg group significantly more important than in the placebo group (diff=-2.5 a.u).

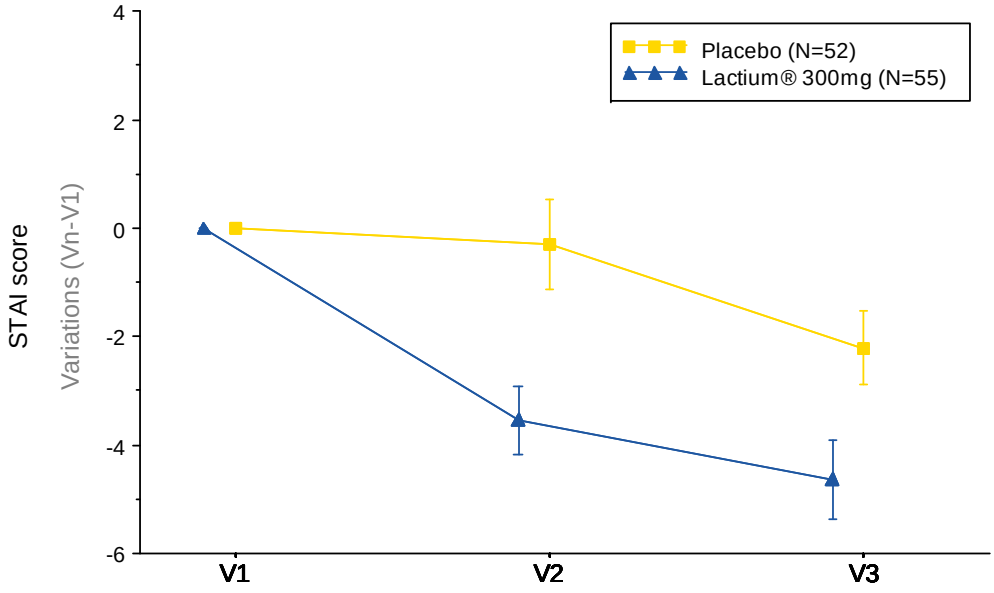

Figure 18: Evolution of STAI questionnaire score (variation from V1)

4.5 Questionnaire of global satisfaction

4.5.1 Convenience of the product

At V3, the following question was asked to the subjects: “Do you think that the product was practical (packaging, conservation, size of the box)?”. The possible answers were “Yes” or “No”.

The resulting answers are presented below.

Table 13: *Convenience of the product*

Product	N	Yes	No
Placebo	52	49 (94.23%)	3 (5.77%)
Lactium® 300mg	55	54 (98.18%)	1 (1.82%)

Except one subject, all the subjects of Lactium® 300 mg group considered that the product was convenient (98.18%, N=54/55).

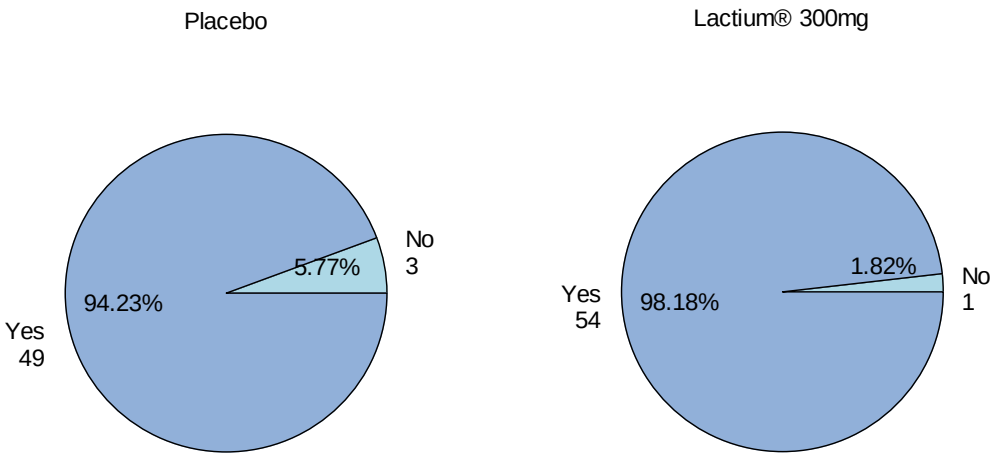

Figure 19: **Convenience of the product**

4.5.2 Directions for use

At V3, the following question was asked to the subjects: “How do you evaluate the directions for use (1 capsule per day in the evening, around 1 hour before going to bed)?”. The possible answers were “Very easy”, “Easy”, “Restricting” or “Very restricting”.

The resulting answers are presented below.

Table 14: *Directions for use*

Product	N	Very easy	Easy	Restricting	Very restricting
Placebo	52	19 (36.54%)	28 (53.85%)	5 (9.62%)	0 (0%)
Lactium® 300mg	55	19 (34.55%)	30 (54.55%)	6 (10.91%)	0 (0%)

The majority of the subjects of Lactium® 300 mg group has considered that the direction for use were at least easy to respect (89.1%, N=49/55)

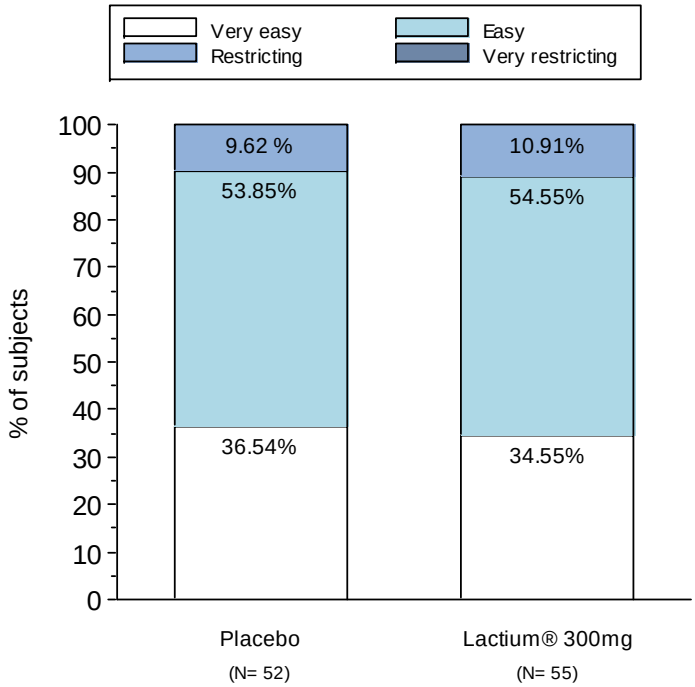

Figure 20: **Directions for use**

4.5.3 General appearance of the product

At V3, the following question was asked to the subjects: “What do you think about general appearance (color, size taste, odor of the capsule) of this dietary supplement?”. The possible answers were “Very satisfying”, “Satisfying”, “Quite satisfying” or “Not satisfying”.

The resulting answers are presented below.

Table 15: *General appearance of the product*

Product	N	Very satisfying	Satisfying	Quite satisfying	Not satisfying
Placebo	52	17 (32.69%)	30 (57.69%)	4 (7.69%)	1 (1.92%)
Lactium® 300mg	55	17 (30.91%)	31 (56.36%)	6 (10.91%)	1 (1.82%)

Almost all the subjects of Lactium® 300 mg group were satisfied with the appearance of the product (87.3%, N=48/55).

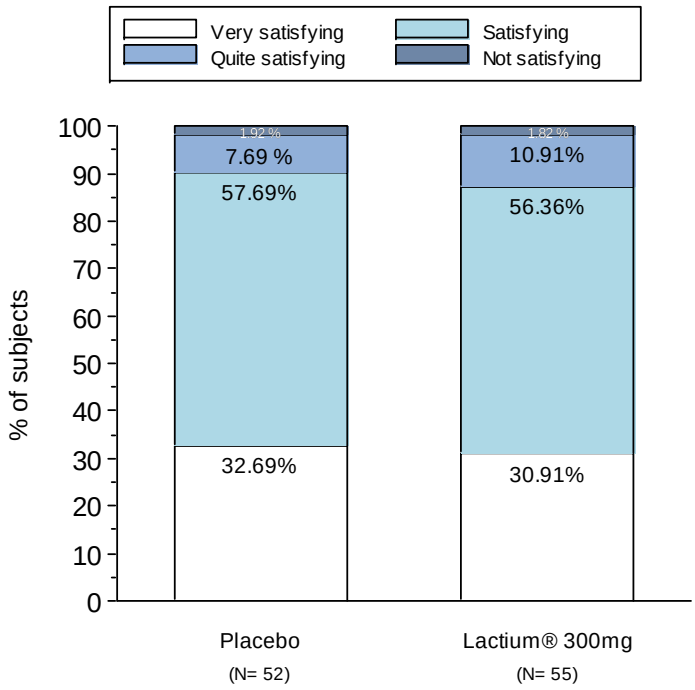

Figure 21: General appearance of the product

4.5.4 Feeling of being less stressed

At V3, the following question was asked to the subjects: “From the beginning of product consumption, do you have the feeling that you are less stressed?”. The possible answers were “A lot”, “Moderately”, “Lightly” or “Not at all”.

The resulting answers are presented below.

Table 16: *Feeling of being less stressed*

Product	N	A lot	Moderately	Lightly	Not at all
Placebo	52	1 (1.92%)	8 (15.38%)	19 (36.54%)	24 (46.15%)
Lactium® 300mg	55	1 (1.82%)	13 (23.64%)	16 (29.09%)	25 (45.45%)

Half of the subjects of Lactium® 300 mg group felt less stressed at the end of the study (54.5%, N=30/55).

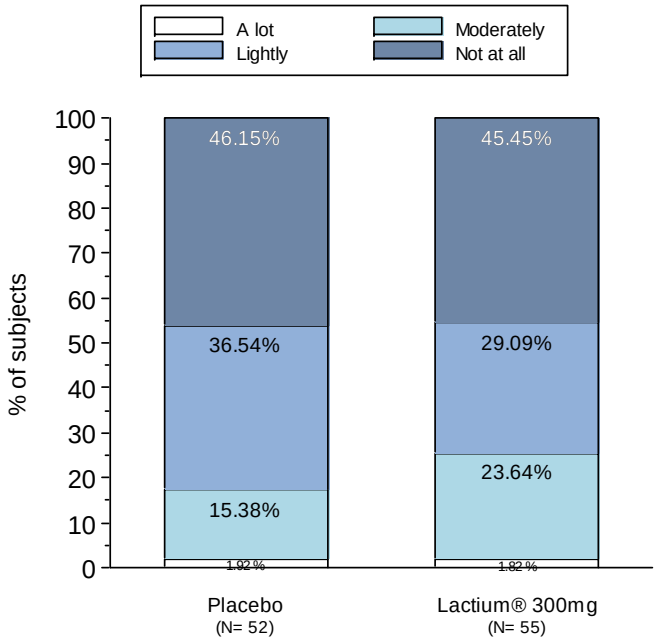

Figure 22: **Feeling of being less stressed**

4.5.5 Feeling of better management of stress

At V3, the following question was asked to the subjects: “From the beginning of product consumption, do you have the feeling that you manage your stress better?”. The possible answers were “A lot”, “Moderately”, “Lightly” or “Not at all”.

The resulting answers are presented below.

Table 17: *Feeling of better management of stress*

Product	N	A lot	Moderately	Lightly	Not at all
Placebo	52	1 (1.92%)	11 (21.15%)	21 (40.38%)	19 (36.54%)
Lactium® 300mg	55	5 (9.09%)	10 (18.18%)	20 (36.36%)	20 (36.36%)

More than half of the subjects of Lactium® 300 mg group felt they have better managed their stress at the end of the study (63.6%, N=35/55)

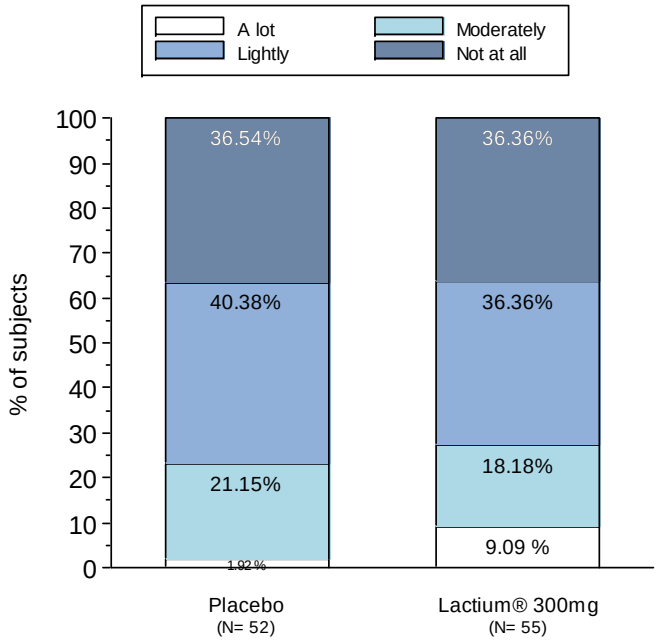

Figure 23: **Feeling of better management of stress**

4.5.6 Quality of sleep

At V3, the following question was asked to the subjects: “From the beginning of product consumption, did the quality of your sleep improve?”. The possible answers were “A lot”, “Moderately”, “Lightly” or “Not at all”.

The resulting answers are presented below.

Table 18: *Quality of sleep*

Product	N	A lot	Moderately	Lightly	Not at all
Placebo	52	5 (9.62%)	9 (17.31%)	15 (28.85%)	23 (44.23%)
Lactium® 300mg	55	7 (12.73%)	11 (20.00%)	12 (21.82%)	25 (45.45%)

Half of the subjects of Lactium® 300 mg group felt their quality of sleep improved at the end of the study (54.5%, N=30/55).

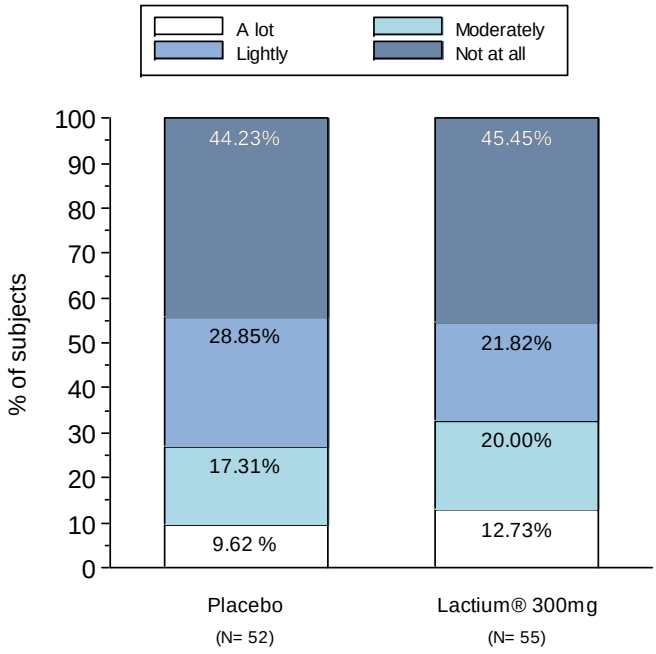

Figure 24: **Quality of sleep**

4.5.7 Feeling of being more dynamic

At V3, the following question was asked to the subjects: “From the beginning of product consumption, do you feel more dynamic?”. The possible answers were “A lot”, “Moderately”, “Lightly” or “Not at all”.

The resulting answers are presented below.

Table 19: *Feeling of being more dynamic*

Product	N	A lot	Moderately	Lightly	Not at all
Placebo	52	4 (7.69%)	10 (19.23%)	10 (19.23%)	28 (53.85%)
Lactium® 300mg	55	7 (12.73%)	11 (20.00%)	9 (16.36%)	28 (50.91%)

Nearly half of the subjects of Lactium® 300 mg group felt more dynamic at the end of the study (49.1%, N=27/55).

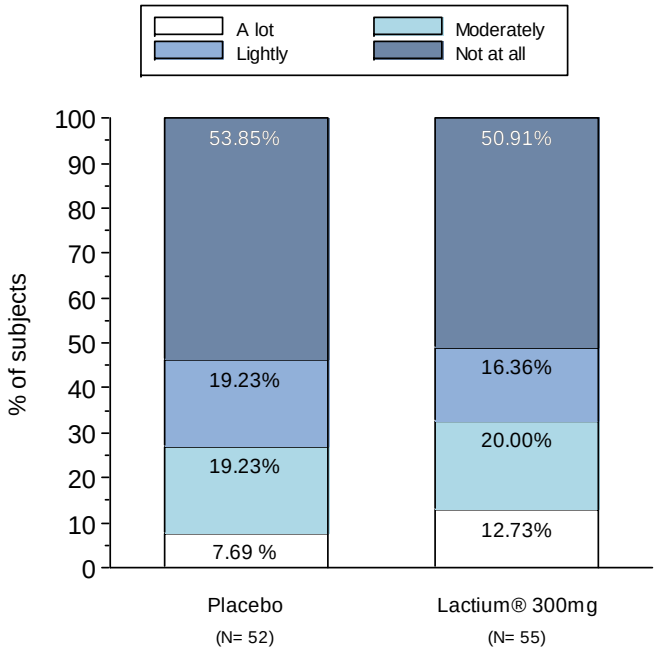

Figure 25: **Feeling of being more dynamic**

4.5.8 Feeling of being more motivated

At V3, the following question was asked to the subjects: “From the beginning of product consumption, do you feel more motivated?”. The possible answers were “A lot”, “Moderately”, “Lightly” or “Not at all”.

The resulting answers are presented below.

Table 20: *Feeling of being more motivated*

Product	N	A lot	Moderately	Lightly	Not at all
Placebo	52	1 (1.92%)	12 (23.08%)	15 (28.85%)	24 (46.15%)
Lactium® 300mg	55	5 (9.09%)	9 (16.36%)	14 (25.45%)	27 (49.09%)

Half of the subjects of Lactium® 300 mg group felt more motivated at the end of the study (50.9%, N=28/55).

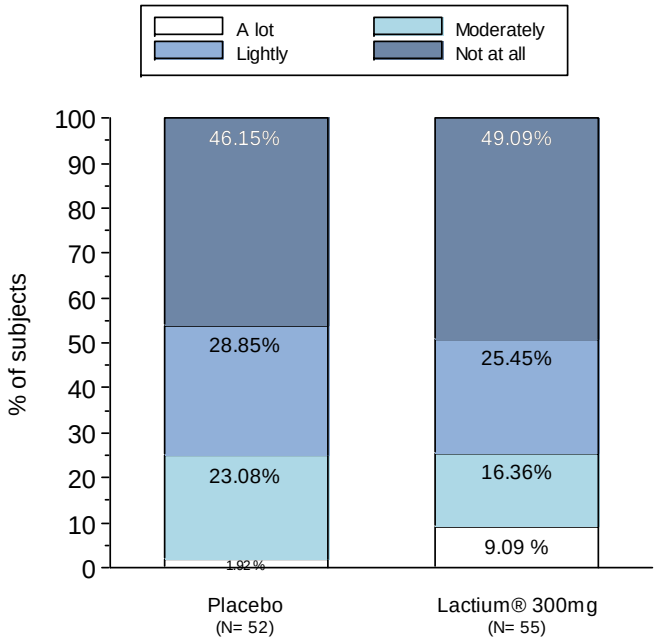

Figure 26: **Feeling of being more motivated**

4.5.9 Feeling of being less irritable

At V3, the following question was asked to the subjects: “From the beginning of product consumption, do you feel less irritable?”. The possible answers were “A lot”, “Moderately”, “Lightly” or “Not at all”.

The resulting answers are presented below.

Table 21: *Feeling of being less irritable*

Product	N	A lot	Moderately	Lightly	Not at all
Placebo	52	2 (3.85%)	14 (26.92%)	10 (19.23%)	26 (50.00%)
Lactium® 300mg	55	6 (10.91%)	8 (14.55%)	19 (34.55%)	22 (40.00%)

More than half of the subjects of Lactium® 300 mg group felt less irritable at the end of the study (60.0%, N=33/55).

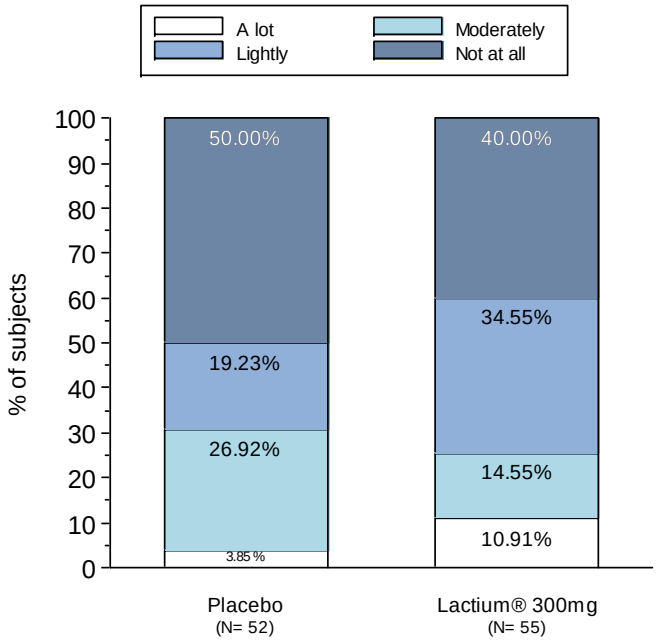

Figure 27: **Feeling of being less irritable**

4.5.10 Relationship

At V3, the following question was asked to the subjects: “From the beginning of product consumption, did your contacts with other people improve?”. The possible answers were “A lot”, “Moderately”, “Lightly” or “Not at all”.

The resulting answers are presented below.

Table 22: *Relationship*

Product	N	A lot	Moderately	Lightly	Not at all
Placebo	52	1 (1.92%)	7 (13.46%)	9 (17.31%)	35 (67.31%)
Lactium® 300mg	55	3 (5.45%)	13 (23.64%)	9 (16.36%)	30 (54.55%)

Nearly half of the subjects of Lactium® 300 mg group considered their contacts with other people have improved at the end of the study (45.5%, N=25/55).

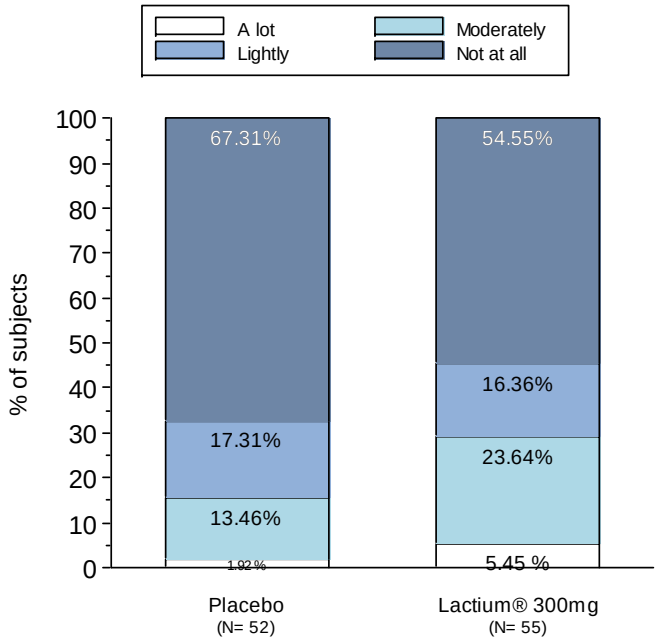

Figure 28: Relationship

4.5.11 Feeling of being better physically

At V3, the following question was asked to the subjects: “From the beginning of product consumption, do you feel physically better?”. The possible answers were “A lot”, “Moderately”, “Lightly” or “Not at all”.

The resulting answers are presented below.

Table 23: *Feeling of being physically better*

Product	N	A lot	Moderately	Lightly	Not at all
Placebo	52	5 (9.62%)	7 (13.46%)	16 (30.77%)	24 (46.15%)
Lactium® 300mg	55	4 (7.27%)	8 (14.55%)	15 (27.27%)	28 (50.91%)

Nearly half of the subjects of Lactium® 300 mg group felt physically better at the end of the study (49.1%, N=27/55).

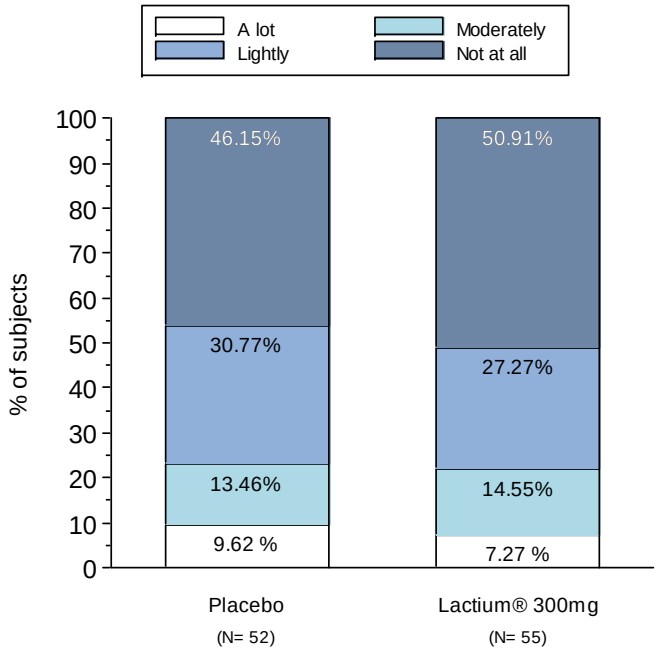

Figure 29: **Feeling of being better physically**

4.5.12 Tolerance of the product

At V3, the following question was asked to the subjects: “How do you assess the tolerance of the product?”. The possible answers were “Excellent”, “Good”, “Average” or “Bad”.

The resulting answers are presented below.

Table 24: *Tolerance of the product*

Product	N	Excellent	Good	Average	Bad
Placebo	52	25 (48.08%)	25 (48.08%)	2 (3.85%)	0 (0%)
Lactium® 300mg	55	26 (47.27%)	27 (49.09%)	1 (1.82%)	1 (1.82%)

Almost all the subjects of the Lactium® 300 mg group had positive opinion on product tolerance (96.4%, N=53/55).

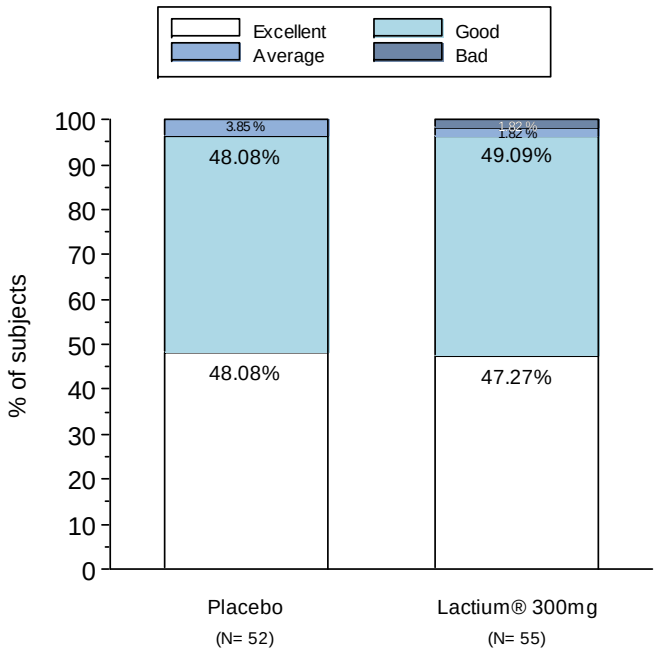

Figure 30: **Tolerance of the product**

4.5.13 Satisfaction with the product

At V3, the following question was asked to the subjects: “Globally, were you satisfied with the product consumed during 6 weeks?”. The possible answers were “Yes” or “No”.

The resulting answers are presented below.

Table 25: *Satisfaction with the product*

Product	N	Yes	No
Placebo	52	37 (71.15%)	15 (28.85%)
Lactium® 300mg	55	37 (67.27%)	18 (32.73%)

Two thirds of the subjects of the Lactium® 300 mg group were satisfied with the product (67.3%, N=37/55).

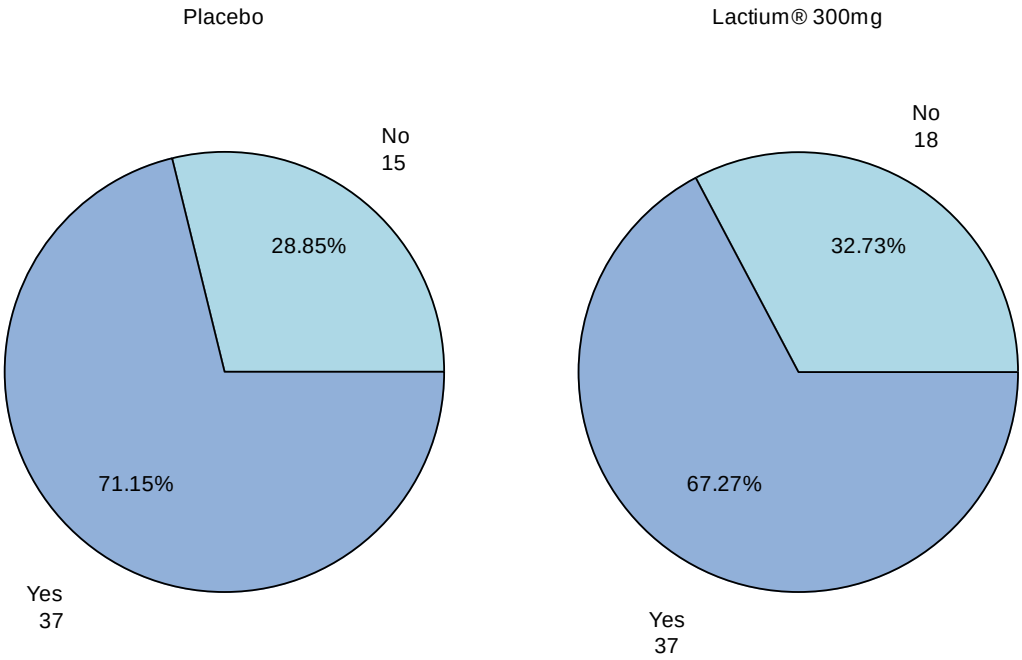

Figure 31: **Satisfaction with the product**

4.5.14 Purchase intention

At V3, the following question was asked to the subjects: “Would you be willing to buy this product?”. The possible answers were “Yes” or “No”.

The resulting answers are presented below.

Table 26: *Purchase intention*

Product	N	Yes	No
Placebo	52	23 (44.23%)	29 (55.77%)
Lactium® 300mg	55	27 (49.09%)	28 (50.91%)

Less than half of the subjects of Lactium® 300 mg be willing to buy with the product (49.1%, N=27/55).

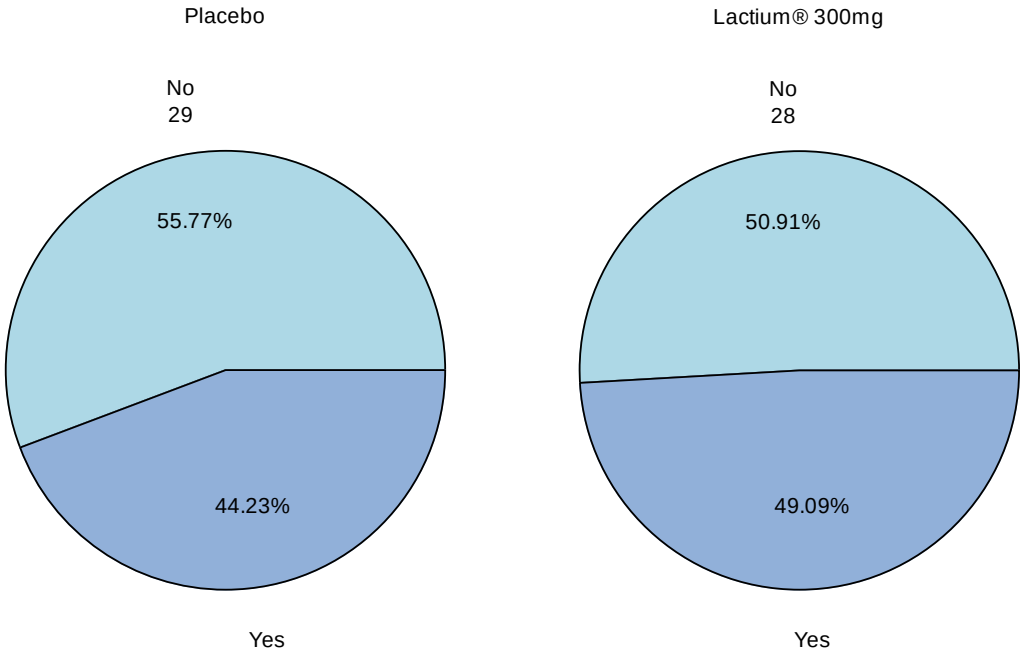

Figure 32: **Purchase intention**

4.5.15 Recommendation to use

At V3, the following question was asked to the subjects: “Would you recommend the use of this product?”. The possible answers were “Yes” or “No”.

The resulting answers are presented below.

Table 27: *Recommendation to use*

Product	N	Yes	No
Placebo	52	29 (55.77%)	23 (44.23%)
Lactium® 300mg	55	33 (60.00%)	22 (40.00%)

Around half of the subjects of Lactium® 300 mg group would recommend the use of the product (60.0%, N=33/55).

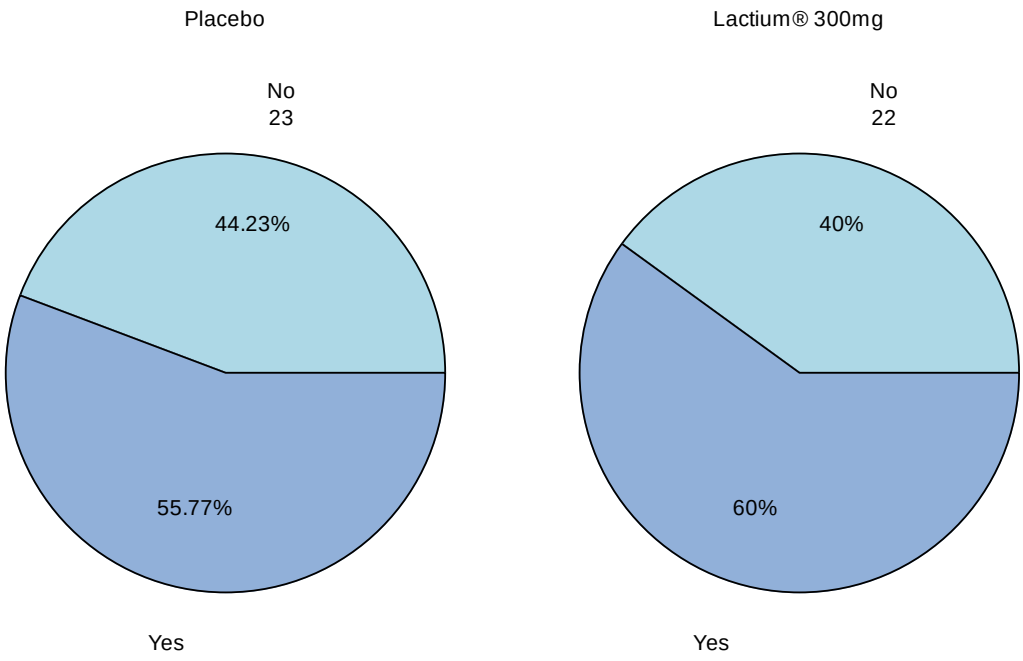

Figure 33: Recommendation to use

5 Discussion and conclusion

The objective of the clinical trial was to study the effect of Lactium® on stress. One hundred and seven healthy adult subjects were recruited and consumed either Lactium® at dose 300 mg or placebo for 6 weeks. The effect of Lactium® on acute stress was studied during an induced stress (Stroop test) and chronic stress was evaluated using a questionnaire (STAI questionnaire). Both were evaluated after 2 weeks (V2) and 6 weeks (V3) of consumption.

Considering the effect of Lactium® on acute stress, statistical analysis showed no reactivity of SPB to induced stress. This absence of reactivity is linked to a positive evolution of SBP between rest and stress situation in both groups (placebo and Lactium® 300 mg): whatever the product consumed, the difference between SBP during rest situation and mean SBP during the induced stress significantly decreased in the two groups between V1 and V3. No effect of Lactium® was either observed during the study on the second data of blood pressure (DBP). Even if no reactivity of heart rate to induce stress was highlighted during the study, a significant product effect at V2 was observed on the difference between heart rate at rest and heart rate 3 minutes and 6 minutes after the induced stress (respectively p=0.0041 and p=0.0399). This observation may be interpreted as a better recovery of heart rate after induced stress after consumption of Lactium® 300 mg compared to placebo. Endly, no reactivity to induce stress was observed considering salivary cortisol concentration and Stroop test scores.

Analysis on chronic stress via STAI questionnaire showed a significant product effect at V2 (p=0.0143): the decrease in STAI score was significantly more important in the group consuming Lactium® 300 mg than in the placebo group.

The positive evolutions observed in the two groups using statistical intragroup analysis highlight a training effect and do not permit to create a product effect of Lactium®.