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AZIENDA OSPEDALIERA SAN MARTINO
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Erogazione di Servizi di Dietetica e Nutrizione Artificiale Enterale e Parenterale

Treatment of anxiety and sleep disturbances

Double blind clinical study with *Cyracos* vs. placebo

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INTRODUCTION

Frequently overweight subjects suffer from anxiety and, in a number of cases, from related sleep disturbances.

It is well known how a negative appreciation of body image induces an emotional state of unease, because the subject foretells a mostly negative opinion from other people about him- or herself.

Such expectation of negative opinions provokes a steering of the emotional colour towards anxiety. Anxiety, and the often related insomnia, are rather frequent pathological occurrences in these cases. (According to the Statistics Institutes, medical examinations are about 30,000/year.) Anxiety can be defined as a feeling of danger, or of a loss against which there is non defence: simply "it must happen".

Therefore, anxiety is a continuous emotional tension towards an imaginary danger or loss. (In this sense it is different from fear, where the danger is real, fear being related to an actual danger.)

Anxiety can direct itself towards affections, work, other's opinion about the physical appearance, health and, generally, life. (R. Rossini, *Trattato di Psichiatria*, 2nd rev. ed., Cappelli Editore, 1972)

By consequence, anxiety is characterized by:

- Psychic symptoms: tension, agitation, dread, apprehension
- Physical symptoms: sweating, fauces' dryness, tremor, palpitations, chest pain, abnormal visceral motility
- Continuous presence.

From case to case one or the other symptom will be prevalent.

As a matter of fact, there is a strong connection with the normal emotions: the quality of what makes one feel an emotion is both psychically and physically very similar to anxiety, though in anxiety quantity is much bigger, abnormal also as to its duration.

According to Freud at the root of this phenomenon lies an unresolved contrast: the ego (the individual, Es) cannot carry out what the instinctive pulsions (Es) want because of the rules and moral and social censures (Superego). Such clash between desire and impossible realisation gives rise to suffering (fear of having-not, loss, lack of consideration, etc.), and anxiety shifts on the outer world (on an imaginary danger) the cause of pain.

As this imaginary danger gives rise to a continuous, all-day-long "fear", it certainly does not favour sleep. This is why anxiety is so often associated with insomnia.

Such connections can hardly surprise: a normal subject having worries is more prone to bother over his or her harassing problems than to catching sleep. As a consequence sleep comes late, breaks off, is short. It happens the same in anxiety. In order to treat the paring anxiety/insomnia we can resort full hands to a cupboard of pharmaceuticals filled with ansiolytic and hypnoinducing molecules.

Nevertheless, problems related to undesired effects are not rare at all: tolerance, dependence, paradoxical reactions, rebound effects, amnesia, attenuate vigilance, interaction with other drugs, hepato- and nephrotoxicity, extrapyramidal syndromes, muscular weakness, etc. (see the *Repertorio farmaceutico*, REFI, in relation to the products of this class.)

Taking this into account, the therapy should not last very long, as suggested by the notices attached to the various commercial specialties, even if in many cases the illness does not show a quick remission. (See Rossini, *op. cit.*) Ansiolytics and psychopharmaceuticals usually enjoy big commercial success; this is because the results asked for by the physician are always the ones of the next drug (higher efficacy, lower collateral effects). For long-term treatments vegetal derivatives (e.g., from valerian, lime-blossoms, passiflora) have also been put to use because the efficacy is accompanied by scarce collateral effects (Vorbach E. U. et al., 1996; Bonin A. V. et al., 1997; Viola H. et al., 1994).

An active component able to treat anxiety, related physical effects and insomnia, should certainly be included in the treatment of the anxiety neurosis and sleep disturbances. This is the case of Melissa with 5% of hydrossicynnamic acid (C.F.M. data on file). It is therefore a product based on Melissa, *Cyracos*, that has called our interest in order to check its ability to mitigate anxiety and improve the sleep in subjects under treatment for weight problems.

In the preparation we have studied, Melissa with 5% of hydrossicynnamic acid is described as able to exert sedation and an anti-stress effect (Soulimani R., Fleurent, Pelt J. M., Laboratoire de Pharmacognosie, University of Metz, France). A visceral antispastic activity has benn reported too (*Bundesanzeiger*, nr. 228 of dec. 5 1984; nr. 50 of march 13, 1990).

MATERIALS AND METHODS

We have enrolled 30subjects and, by a random choice, treated 20 of them with *Cyracos*, while 10 were given a placebo.

Packages were all identical and numbered, each box containing 30 tablets of either *Cyracos* or placebo.

Each subject was given a box at time 0 (T0), in accordance with a therapeutic cycle of 15 days (2 tablets a day).

Cyracos: composition by decreasing weight order (1 tab = mg 0.450)

MELISSA EXTR.	66,67%
MALTODESTRINE	18,89%
MICROCRYSTALLINE CELLULOSE	11,11%
STEARATE MAGNESIUM	1,56%
TALC	1,11%
MICRONIZED SILICA	0,67%

Placebo: composition by decreasing weight order (1 tab = mg 0.450)

HOP	66,67%
MALTODESTRINE	18,89%
MICROCRYSTALLINE CELLULOSE	11,11%
STEARATE MAGNESIUM	1,56%
TALC	1,11%
MICRONIZED SILICA	0,67%

The study lasted 30 days since the admittance of the first patient.

PATIENTS AND SELECTION CRITERIA

Our study comprised of 30 subjects of both sexes, aged between 18 and 70, randomly assigned to the two groups: *Cyracos* was administered to the one composed of 20 subjects, while the other one was given a placebo.

The patients affected by anxiety neurosis and sleep disturbances underwent to contemporary dietetic treatment and assumed a lipase inhibitor for weight control (overweight with BMI between 25 and 30). They were homogeneous as to age, weight, intensity of anxiety's and related symptoms, and sleep disturbances.

EXCLUSION CRITERIA

- Assumption of anti-anxiety drugs, antidepressants, hypnoinducers and, in general, sedatives, in the 10 days before the beginning of our study

- Diabetes
- Asthma
- Hyperthyroidism
- Depression
- Severe obsessive-compulsive disturbance
- Schizophrenia
- Psychosis in general
- Serotonine-reuptake inhibitors drugs (SRI)

TREATMENT AND POSOLOGY

All subjects have combined the dietetic prescriptions and the chelant with the *Cyracos* for 15 days: a tablet in the morning (at 10:00 a.m.) and another one in the evening (before sleeping).

DATA COLLECTION SCHEDULE AND EVALUATION PARAMETERS

On first medical examination we have registered:

- Age, weight, sex
- Clinical status of the anxiety neurosis at the time of admittance in the study:
  - Anxiety manifestations (for each a scale from 0 to 3)
  - Correlated symptoms (for each symptom a scale from 0 to 3)
  - Initial insomnia (for each datum a scale from 0 to 3)
  - Central insomnia (for each datum a scale from 0 to 3)
  - Terminal insomnia (for each datum a scale from 0 to 3)

DETECTED VARIABLES

Level of anxiety manifestations	(T0-T15)
Level of anxiety symptoms	(T0-T15)
Level of sleep disturbances	(T0-T15)
Compliance	(T15)
Collateral effects	(T15)

EFFICACY EVALUATION

At the end of the treatment, we have evaluated, the clinical efficacy of the active product vs. the placebo. To this purpose we have compared the initial conditions of each subject with the ones at the end of the treatment in terms of anxiety neurosis' manifestations, associated symptoms and insomnia. The efficacy has been defined by means of principal and secondary end-points.

ANALYSIS

We have analysed the following data:

- Age at T0
- Weight at T0
- Sex at T0
- Severity of anxiety neurosis and insomnia at T0
- Severity of anxiety neurosis and insomnia at T15
- Severity of anxiety neurosis and insomnia at T15 vs. T0

- Global results at T15
- Compliance at T15
- Collateral effects at T15

Therefore, we have evaluated both the homogeneity of our two groups and the possible meaningfulness of the variations observed between T0 and T15 in the groups. Meanwhile, we have checked the global results at T15 for both groups.
The evaluation of the efficacy has been performed for all subjects completing the study (drop-outs being replaced by reserves), while the evaluation of collateral effects for all enrolled people.

TEST

We have employed Student's T-test, with meaningfulness set at p=0.05.

RESULTS

The results drawn from the tables, based on the schedules, come from the behaviour of anxiety's and insomnia's manifestations and symptoms between beginning and end of treatment, i.e., between T0 and T15.Global result refer to the last medical examination, i.e., at T15. As to compliance and collateral effects T15 data have been examined, while homogeneity has been established on the values at T0.

HOMOGENEITY
Summary Table of Measured Data for ACTIVE and PLACEBO GROUPS

	ACTIVE GROUP		PLACEBO GROUP		
	T0		T0		P
Variable	*Value*	*s.d.*	*Value*	*s.d..*	
Age	44,05	14,40	48	13,5	0,49 ns
Weight	79,47	19,05	77	16,3	0,71 ns
Sex	70% F		70% F		0,05 ns
ANXIETY MANIFESTATIONS					
Agitation	1,3	0,71	0,5	0,67	0,08 ns
Excessive activity	0,4	0,49	0,4	0,49	0,1 ns
Motility disturbances	0,45	0,67	0,1	0,3	0,13 ns
Tension	0,7	0,78	0,4	0,49	0,32ns
ASSOCIATED SYMPTOMS					
Difficulty with food (weight)	1,6	0,97	1,2	0,75	0,27 ns
Emotional instability (hostility)	0,25	0,54	0,1	0,3	0,43 ns
Asthenia	0,8	0,87	0,2	0,4	0,055 ns
Guilt feelings (remorse)	0,65	0,85	0,2	0,6	0,16 ns
Inferiority feelings (inhibitions)	0,8	0,87	0,1	0,3	0,2 ns
Mental confusion (indecision)	0,5	0,74	0,4	0,49	0,2 ns
Muscular reactions (contractions)	0,5	0,67	0,5	0,67	0,3 ns
Compulsory obsessive behaviour	0,35	0,79	0,3	0,79	0,18 ns
Poor relationships with others (dysadaptation)	0,65	1,08	0,2	0,4	0,2 ns
Psychosomatic perturbations (hemicrania etc.)	1,05	0,8	0,7	0,64	0,25 ns
Dermatological reactions (cutaneous striae)	0		0		
Speaking difficulties (stammering)	0,1	0,3	0,1	0,3	0,31 ns
Somatic disturbances (hypochondria)	0,5	0,67	0,41	0,66	0,71 ns
INSOMNIA					
1. Initial	1,55	0,5	1,3	0,46	0,2 ns
2. Central	1,2	0,6	1,1	0,54	0,67 ns
3. Terminal	1,65	0,73	0,6	0,66	0,86 ns

Anxiety: intensity, manifestation and symptoms (0=absent, 1=light, 2=moderate, 3=severe)
Initial insomnia: difficulty (0=none, 1=sometimes, 2=always)
Central insomnia: difficulty (0=none, 1=restlessness, 2=night awakening)
Retarded insomnia: difficulty (0=none, 1=premature dawn awakening followed by sleep, 2=final awakening at dawn)
Global results at last examination (1=excellent, 2=good, 3=fair, 4=poor, 5=worsening)

The statistical analysis shows the homogeneity of both groups.

EFFICACY
Summary Table of Measured Data for ACTIVE and PLACEBO GROUPS

	ACTIVE GROUP					PLACEBO GROUP				
	T0	s.d.	T15	s.d.	P	T0	s.d.	T15	s.d.	P
ANXIETY MANIFESTATIONS										
Agitation	1,3	0,71	0,25	0,43	0,0000029 *	0,5	0,67	0,6	0,66	0,75ns
Excessive activity	0,4	0,49	0		0,007*	0,4	0,49	0,1	0,3	0,7ns
Motility disturbances	0,45	0,67	0,005	0,22	0,017*	0,4	0,49	0,4	0,39	1ns
Tension	0,7	0,78	0,15	0,36	0,008*	0,4	0,49	0,3	0,31	0,7ns
ASSOCIATED SYMPTOMS										
Difficulty with food (weight)	1,6	0,97	0,6	0,66	0,00065*	1,2	0,75	1,1	0,83	0,79ns
Emotional instability (hostility)	0,25	0,54	0,05	0,22	0,014*	0,1	0,3	0,1	0,3	1 ns
Asthenia	0,8	0,87	0,25	0,43	0,018*	0,2	0,41	0,2	0,4	1ns
Guilt feelings (remorse)	0,65	0,85	0,15	0,36	0,02*	0,2	0,6	0,4	0,66	0,51ns
Inferiority feelings (inhibitions)	0,8	0,87	0,25	0,43	0,02*	0,1	0,3	0,1	0,3	1ns
Mental confusion (indecision)	0,5	0,74	0,2	0,4	0,000083*	0,4	0,49	0,1	0,3	0,13ns
Muscular reactions (contractions)	0,5	0,67	0,1	0,3	0,02*	0,5	0,67	0,4	0,66	0,35ns
Compulsory obsessive behaviour	0,35	0,79	0,2	0,51	0,49ns	0,3	0,79	0,2	0,69	0,40ns
Poor relationships with others (dysadaptation)	0,65	0,08	0,25	0,62	0,15ns	0,2	0,4	0,2	0,6	1ns
Psychosomatic perturbations (hemicrania etc.)	1,05	0,8	0,05	0,22	0,0000065 *	0,7	0,64	0,6	0,66	0,75ns
Dermatological reactions (cutaneous striae)	0	0	0	0	0	0				
Speaking difficulties (stammering)	0,1	0,3	0	0,15ns	0,1	0,3	0,2	0,4	0,6ns	
Somatic disturbances (hypochondria)	0,5	0,67	0,25	0,43	0,18ns	0,41	0,6	0,5	0,67	0,75ns
INSOMNIA										
1. Initial	1,55	0,5	0,55	0,5	0,0000003 *	1,3	0,46	1,4	0,49	0,66ns
2. Central	1,2	0,6	0,3	0,46	0,0000012 *	1,1	0,54	0,7	0,64	0,17ns
3. Terminal	1,65	0,73	0,1	0,3	0,0041*	0,6	0,66	0,2	0,4	0,14ns
GLOBAL RESULTS (LAST EXAMIN.)		**1**							**3,4**	**0,001***
COMPLIANCE: Nr of unused tabs at T15	**0**		**0**	**0**						
COLLATERAL EFFECTS at T15		0		0	0					

* = significant ns = non-significant

Anxiety: intensity, manifestation and symptomatology (0=absent, 1=light, 2=moderate, 3=severe)
Initial insomnia: difficulty (0=none, 1=sometimes, 2=always)
Central insomnia: difficulty (0=none, 1=restlessness, 2=night awakening)
Retarded insomnia: difficulty (0=none, 1=premature dawn awakening followed by sleep, 2=final awakening at dawn)
Global results at last examination (1=excellent, 2=good, 3=fair, 4=poor, 5=worsening)
The statistical analysis shows the homogeneity of both groups.

The difference between the clinical conditions before and after the treatment in the "active" group shows a very high efficacy of the tested product. Such efficacy is not accidental but statistically significant, well over the threshold of 0.05. The product appears effective on insomnia, all anxiety manifestations and a number if associated symptoms, excluding the ones of special kind for which a treatment with ansiolytic alone is not recommended.

DISCUSSION AND CONCLUSIONS

Talking into account that cases of anxiety with insomnia are frequent in subjects with problems related to an inadequate nutrition both in quality and quantity, and that a therapy with ansiolytic drugs though active can have undesired or in any case unlooked for effects, we deem that the results of our study are encouraging.

CYRACOS – DATA COLLECTION SCHEDULE

Pateint's initials .... Age... Weight.... Sex M F (thick appr.) Admittance Nr.....
Nr. Of the treatment box.....

Overweight Therapy
.....

Anxiety neurosis/ sleep disturbances therapy
.....

Beginning of treatment date ..... Posology
.....

Symptoms	T0	T15
ANXIETY MANIFESTATIONS		
Agitation	0 1 2 3	0 1 2 3
Excessive motility	0 1 2 3	0 1 2 3
Motilità disturbances	0 1 2 3	0 1 2 3
Tension	0 1 2 3	0 1 2 3
ASSOCIATED SYMPTOMS		
Difficulty with food (weight)	0 1 2 3	0 1 2 3
Emotional instability (hostility)	0 1 2 3	0 1 2 3
Asthenia	0 1 2 3	0 1 2 3
Guilt feelings (remorses)	0 1 2 3	0 1 2 3
Inferiority feelings (inhibitions)	0 1 2 3	0 1 2 3
Mental confusion (indecision)	0 1 2 3	0 1 2 3
Muscular reactions (contractions)	0 1 2 3	0 1 2 3
Compulsive obsessive behaviour	0 1 2 3	0 1 2 3
Poor relationships with others (dysadapt.)	0 1 2 3	0 1 2 3
Psychosomatic perturbations (hemicrania)	0 1 2 3	0 1 2 3
Dermatologic reactions (cutaneous striae)	0 1 2 3	0 1 2 3
Speaking difficulties (stammering)	0 1 2 3	0 1 2 3
Somatic disturbances (hypocondria)	0 1 2 3	0 1 2 3

INTENSITY (thick) 0 = absent, 1= light, 2 = moderate , 3 = serious

INSOMNIA

1) Initial (thick appr. value) 0 1 2 0 1 2
0 = no difficulty, 1 = sometimes difficulties (30'/45' to catch sleep), 2 = always difficulties

2) Central (thick appr. value) 0 1 2 0 1 2
0 = no difficulty, 1 = night unrest, 2 = awakening in the night

3) Terminal (thick appr. value) 0 1 2 0 1 2
0 = no difficulty, 1 = early awakening (dawn) followed by sleep, 2 = final awakening at dawn

GLOBAL RESULTS (LAST EXAMINATIONS)
0 = excellent, 2 = good , 3 = fair, 4 = poor, 5 = worsening (thick as appr.)

COMPLIANCE: Nr. Of unused tabs at T15 .....

COLLATERAL EFFECTS at T15
.....

ACTIVE GROUP

	A		B		C		D		E		F		G		H		I		L		M		N		O		P		Q		R		S		T		U		V		RG	EC/C	
	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	T15	T15
PS	2	1	1	0	0	0	2	1	3	1	2	1	0	0	0	0	0	0	1	0	2	1	1	0	2	0	2	0	0	0	1	0	2	1	2	1	2	0	0	0	1	0	0
OD	1	0	0	0	1	0	0	0	3	1	1	0	3	1	3	1	3	1	3	1	0	0	3	2	3	2	1	0	0	0	0	0	0	0	2	1	0	0	0	0	1	0	0
AN	2	0	1	0	2	0	1	0	0	0	1	0	1	0	0	0	1	0	1	0	1	0	0	0	0	0	2	0	0	0	0	0	0	0	1	0	1	0	0	0	1	0	0
PR	2	0	1	0	1	0	1	0	1	0	1	0	2	1	1	0	1	1	2	1	1	0	0	0	1	0	1	0	0	0	0	0	0	0	2	1	2	1	2	0	1	0	0
RR	1	0	0	0	0	0	0	0	2	1	0	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	1	0	1	0	1	0	1	0	0
AM	2	1	0	1	1	0	2	1	3	1	0	0	1	0	2	0	2	1	2	0	2	1	2	1	3	1	3	0	0	0	0	0	0	0	1	0	1	0	1	0	1	0	0
CM	0	0	0	0	2	1	2	0	2	1	0	0	1	0	0	0	0	0	1	0	1	0	1	1	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0
CC	1	0	0	0	0	0	0	0	2	1	0	0	0	0	1	0	1	0	1	0	0	0	0	0	0	0	2	1	0	0	1	0	1	0	2	0	1	0	0	0	1	0	0
DAN	1	0	0	0	0	0	1	0	2	1	0	0	0	0	1	0	1	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2	1	1	0	0	0	1	0	0
GR	2	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	1	0	1	0	0	0	0	0	1	0	0	0	0	0	1	1	2	1	2	0	2	1	1	0	0
GV	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0	1	0	1	0	3	0	0
DRL	1	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	1	0	0	0	1	0	0
FG	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	1	1	0	0	2	0	0
PM	2	1	1	0	1	0	0	0	3	2	0	0	1	1	2	1	2	1	2	1	0	0	0	0	2	2	2	0	0	0	0	0	0	0	2	1	2	1	0	0	2	0	0
PMR	2	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	1	0	1	0	1	1	1	0	0
BM	2	1	0	0	0	1	1	0	1	0	0	0	1	0	1	1	1	0	1	1	1	0	0	0	1	0	1	0	0	0	0	0	1	1	1	1	1	0	1	0	1	0	0
IC	2	1	1	1	0	1	2	0	3	2	0	0	2	1	0	0	2	1	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2	1	2	1	0	0	1	0	0
CLM	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2	1	1	0	1	0	1	0	0
LRC	1	0	1	0	1	0	1	1	1	0	0	0	0	0	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	0	1	0	0
BA	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2	1	2	1	2	0	1	0	0
M T.O	1.3		0.4		0.45		0.7		1.6		1.25		0.8		0.65		0.8		1.05		1.5		1.35		1.65		1.05		0		0.1		0.5		1.55		1.2		0.65					
M T.15	0.25		0		0.005		0.15		0.6		0.05		0.25		0.15		0.25		0.2		0.1		0.2		0.25		0.05		0		0		0.25		0.55		0.3		0.1		1		
DS T.O	0.71		0.49		0.67		0.78		0.97		0.54		0.87		0.85		0.87		0.74		0.67		0.79		1.01		0.8		0		0.3		0.67		0.5		0.6		0.73					
DS T.15	0.43		0		0.22		0.36		0.66		0.22		0.43		0.36		0.43		0.4		0.3		0.51		0.62		0.72		0		0		0.43		0.5		0.46		0.3		1		

DATA T.0/T.15 CONTROL GROUP

	A		B		C		D		E		F		G		H		I		L		M		N		O		P		Q		R		S		T		U		V		RG	EC/C	
	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15	TO	T15		
BM	2	2	1	0	1	0	2	2	1	1	1	1	1	1	0	1	0	0	1	0	1	1	1	1	2	2	1	0	1	0	1	0	0	2	1	0	0	0	3	0	0	
GP	1	1	1	0	0	0	0	0	1	1	0	0	0	0	0	1	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	1	1	1	2	1	1	0	0	4	0	0	
RM	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	1	0	0	1	1	1	0	0	4	0	0	
LA	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	1	0	0	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	1	1	1	1	0	0	3	0	0	
MM	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	1	2	2	0	0	0	4	0	0	
MS	1	1	1	0	0	0	1	1	1	1	0	0	0	0	0	0	1	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	3	0	0	
MD	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	2	0	0	
MS	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	1	0	0	0	3	0	0	
MP	1	1	0	1	0	0	0	1	2	2	0	0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	4	0	0	
MS	0	0	0	1	0	0	0	0	3	3	0	0	1	1	2	2	1	1	1	1	0	0	0	0	1	0	0	0	0	0	0	0	2	2	2	2	0	0	2	1	4	0	0	
M	T.O	T.15	1.5	0.6	0.4	0.3	0.1	0	0.4	0.3	1.2	1.1	0.1	0.1	0.2	0.2	0.2	0.4	0.1	0.1	1.4	0.1	0.5	0.4	0.3	0.2	0.2	0.2	0.4	0.6	0.7	0.6	0	0	0.1	0.2	0.4	0.5	1.3	0.4	1.1	0.7	0.6	0.2	3.4		
DS	T.O	T.15	0.67	0.66	0.49	0.3	0.3	0	0.49	0.31	0.75	0.83	0.3	0.3	0.4	0.4	0.6	0.66	0.3	0.3	0.49	0.3	0.67	0.66	0.79	0.69	0.4	0.6	0.64	0.66	0	0	0.3	0.4	0.66	0.67	0.46	0.49	0.54	0.64	0.64	0.4	2.9		

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In conclusion, the treatment of anxiety and insomnia with melissa (300 mg twice a day) (Cyracos) appears an effective remedy in the short term. Particularly, it has been observed a statistically meaningful effect on anxiety symptoms, with a marked reduction of excitement condition, tension and emotional instability. As to the treatment of insomnia, although effects can be detected in all phases, a relevant efficacy can be ascribed to the first one (in-sleeping phase).

Moreover, melissa (Cyracos) does not present collateral effects and therefore stands for a manageable and sure product.

The placebo group presented and improving trend, though not statistically meaningful, in central and retarded insomnia, which can be attributed to the diet that all patients of the study were undergoing to. The hypocaloric diet actually provoked a reduction of ingesta in both treated groups (either with melissa (Cyracos) or placebo) that could be related to the improvement of the dyspeptic symptoms due to abundant evening meals.

Consequently, it is possible to state that Melissa (Cyracos) represents a herbal remedy both manageable and effective in the treatment of anxiety and sleep troubles.

Prof. S.G.Sukkar