HOMEOPATHIC RESEARCH STUDY ON TITANIUM METALLICUM

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INTRODUCTION

Titanium is a transition element in the periodic table, its symbol is Ti and its Atomic number is 22. It is a silver coloured metal, used principally in the production of light and resistant alloys. It was identified as one of the constituents of rutile (TiO_2) by the German chemist Martin Heinrich Kalproth in 1795, but it was isolated only five years later. It is a part of the composition of many other minerals, it is mainly found in Ilmenite ($FeO\text{-}TiO_2$) and Titanite (sphene) ($CaO\text{-}TiO_2\text{-}SiO_2$). The pure metal is generally obtained through a complicated and costly preparation method, starting from titanium tetrachloride, by making titanium dioxide react with chlorine in an atmosphere of argon, and the resulting product, a pure metal in a spongy state, is melted and stored in bars. Titanium is considered one of the noblest metals due to its excellent qualities. Compared to other materials, it is highly resistant to corrosion, its elasticity module value is very low and also the linear thermal expansion coefficient. It has a low density (about 4.5 kg/cm^3, with minor variations, depending on the type of alloy, equal to 58% of the density of stainless steel) and a very high melting point, equal to 1700° C. It dissolves exclusively in concentrated hydrochloric acid and sulphuric acid, and mainly in hydrofluoric acid, which is its best solvent. It is widely present in nature in the form of oxides, and is contained in a number of minerals. Titanium is the ninth most common element, and is the fourth most abundant metal. It is preceded only by aluminium, iron and magnesium. However its extraction, which is quite complex and costly, became possible only towards the end of the Thirties, after the metallurgist W. J. Kroll invented the process, the difficulties derive from its affinity for elements that are greatly diffused in the air, such as hydrogen, oxygen and nitrogen, which give origin to solid and very stable solutions that are characterized by great hardness and fragility. Modern technologies today enable a vast utilization of titanium in the aerospace sector, and in the medical field, in particular in orthopaedics, vascular surgery and odontology (see implantology). In metallurgy, titanium alloys are used as deoxidizers and denitrifiers, due to their affinity for oxygen and nitrogen. Titanium dioxide is a white pigment (known as titanium white) used in the production of paints, plastic materials, fabrics, paper and rubber.

At present no homeopathic trials are being conducted on titanium, with the exception of 8 symptoms present in Materia Medica, noted by different homoeopathists, probably in different periods from their clinical experience:

1) Vertigo noted by Allen Timothy F.
2) Decreased field of vision noted by Master Farokl J.
3) Hemianopsia noted by Boericke William
4) Horizontal hemianopsia noted by Moffan John
5) Vertical hemianopsia noted by Boericke O. and Scholten Jan
6) Precocious ejaculation noted by Kent J. T. and Vithoulkas G.
7) Involuntary ejaculation noted by Boericke O.
8) Lupus cancer disease noted by Boericke W.

These few symptoms that were recorded, led the "L'Albero della Vita" cultural association in Catania, to conduct a Clinical Trial, in collaboration with Prof. Mario Matera, 1st. Chair of

Pharmacology II of the Department of Experimental and Clinical Pharmacology, Faculty of Medicine and Surgery of the University of Catania.

MATERIALS AND METHODS

For this Trial, a supply of the substance Titanium Metallicum from the Pharmaceutical Company Carlo Erba Italia and then from the Homoeopathic Company IMO in Trezzano Rosa (MI), was used. These were supplied starting from T.M. preparation in 3 batches, one with placebo, 2 with verum in 30 CH and 200 K according to the Rules of Good Homoeopathic Manufacture, as suggested by the Monitor, Prof. Mario Matera, in order to be able to start the Trial. Only the Pharmaceutical Manager of the Company IMO and the Monitor were aware of the different batches. Information about the batches will be known only at the end of the Research Study.

- For the Research Study, 24 volunteers were recruited. They were of both genders (14 males and 10 females), of Caucasian race, and ages varying between 20 and 50 years, weight not exceeding $\pm$20% of the ideal weight indicated in the "Metropolitan Height and Weight" table, a satisfactory state of health, as verified in the preliminary clinical examination, in which the subject's personal data and medical history were recorded. A normal condition with regard to body weight, medical history, ECG, haematological, haematochemical and urinary values.
- Absence of toxicogenic substances and/or participation in other Clinical trials in the three months prior to the start of the subject Research Study.
- Absence of allergic hypersensitivity phenomena or idiosyncrasy to drugs or foodstuffs.
- Absence of alterative symptoms in the cardiovascular, gastroenteric, endocrine apparatuses and in hepatic functionality
- Absence of intake of drugs that the Study doctor, the Investigators and Provers believed might interfere with the homeopathic assessment, during the four weeks prior to the start of the Study.
- Absence of nervous and mental diseases .
- Subjects that were fully able to cooperate and express their voluntary consent, understanding the scope of the study well, and also the methods used to conduct the Research Study.

The Research Study was carried out in the period from June 2003 to February 2004, in accordance with the principles of the Declaration of Helsinki (1964) and the subsequent modifications (Tokyo, 1975 - Venice, 1983 - Hong Kong, 1989) and of good homeopathic practice. Therefore after receiving a detailed description of how the Study would be conducted, the method of administration of the Study drug, the protocol for recording the symptomatology and an adequate information regarding the scopes and risks that the Study could involve, each subject gave his/her explicit consent.

PARTICIPATING STAFF

MONITOR:
Prof. Mario Matera (Department of Experimental and Clinical Pharmacology, University of Catania)

STUDY DOCTOR:
Dr. Maria Francesca Spada (Nutritionist and Homoeopathist - l'Albero della vita Association, Catania)

INVESTIGATORS:
Dr. Gaetano Arena (Geriatrician and Homoeopathist - l'Albero della vita, Catania)
Dr. Riccardo Nocifora (Cardiologist and Homoeopathist, Palermo)

PHARMACEUTICAL MANAGEMENT AND SPONSOR :
Company IMO (Trezzano Rosa - MI)

TRIAL PROTOCOL

The Study was conducted on 24 healthy volunteers, randomized to three groups of 8 subjects each. According to a triple-blind procedure, *verum* was administered to 16 subjects, and *placebo* was administered to 8, at the dose of 3 granules in the morning and in the evening, far from meals, according to the following protocol:

1. Initial screening visit to verify the suitability for recruitment, according to the inclusion and exclusion criteria listed above.
2. Randomization of the voluntary subjects into the groups of treatment, following the Schwartz and coll. method, using the Cochrane and Cox randomization table.
3. Start recording the subjective symptoms for one week.
4. Day of the beginning of the Study. The assigned preparation must be taken for 15 days, and the symptomatology must be recorded daily
5. Self-observation and recording of the subjective symptoms, for 15 more days after the end of the administrations of the Study drug.
6. Interviewing the voluntary participants, a complete medical examination in order to record any undesirable effects and analysis of the observation-cards with the Investigator.

DESCRIPTION OF THE RESEARCH STUDY

In order to check the suitability at the time of recruitment, two weeks before the start of the Study, a preliminary meeting was held, in which a detailed description was made of how the research study would be carried out, and also to describe whatever was connected to the Study. Each volunteer subject was then subjected to a medical examination, and the medical history was recorded according to the homeopathic methods, and laboratory tests were prescribed in order to verify the haematological, haematochemical, urinary and electrocardiographic conditions of each subject.

The volunteers who were recruited were asked to record their symptoms, on specific cards, which were subdivided into three different levels: physical, emotional and mental, for a period of one week before the start of the treatment.
The Provers started to take the remedy (*verum* or *placebo*) in the dose of 3 granules twice a day, for 15 days, continuing to record the symptomatology on a daily basis (according to the Investigator, discontinuation of the treatment was foreseen in case of the onset of new important symptoms).
The period of observation and the related recordings, were continued for 15 more days after the end of the treatment.
Contacts between Provers, Investigators and the Study doctor were scheduled on a daily basis, and the treatment was always discontinued whenever new symptoms appeared.
The cards were then collected, and the entire research group (Investigator, Study doctor and Monitor) met in order to verify the data and carry out a complete analysis of the symptoms pointed out by each of the volunteers.
Lastly the envelope containing the randomization codes was opened, and the results obtained with *verum* or with *placebo* were put together.

TITANIUM METALLICUM PATHOGENESIS

The subjects who took placebo (072) pointed out mild diffused symptoms, which did not last long, which the patients had already noticed during the self-observation period, and which could be correlated to daily conditions, such as a sense of occlusion in the ears and nose, dry throat, dry cough, feeling of heaviness in the head and eyes, diarrhoea liquid stools, urgent need to urinate, mild heaviness in the lower limbs, mild aerophagia 001 (F.L.) – 005 (S.G.) – 015 (A.P.) – 023 (S.C.) – 024 (S.P.). Only Prover 012 (L.L.) experienced widespread itching, between the 5th and 8th day, to the extent that he withdrew from the research study. The other Provers who took placebo did not note any symptoms that were worthy of mention.
The effects of the Research Study, among the volunteers who took *verum,* were noted in a relevant manner with the 200 K dilution (071) and in a less marked manner with the 30 CH dilution (070), on the nervous system, head, mouth, vertigo, eyesight, abdomen, with variations in the alvus, sexual activity

and libido, the extremities, upper and lower limbs, skin and sleep. The symptoms of the 16 *verum* 30 CH and 200 K subjects, were classified into the following groups:

1. New symptom (N.S.)
2. Old symptom (O.S.)
3. Modified symptom (M.S.)
4. Cured Symptom (C.S.)

It was noted that at least 10 Provers experienced symptoms caused by the remedy, that continued for at least 7 days after the remedy was discontinued.

MIND

In 4 subjects who took 200 K (071), very clear mental symptoms were noted. Prover 010 (G.R.) experienced a panic attack in a closed environment (N.S.), from the 10th to the 13th day, a symptom that was noted once again in a parking lot (claustrophobia), with a sense of oppression in the chest, suffocation, and great agitation. Prover 017 (G.P.) noted a marked irritability in the morning, from the 7th to the 10th day, and restlessness accompanied by tension in the solar plexus, without any plausible reason, and a crowding of thoughts regarding unimportant situations (O.S.). Prover 020 (E.D.C.) noted a physical, and especially a mental improvement after the menstrual cycle, which continued for at least one week. She wrote: “I feel more serene in facing the daily problems, with a greater self control and assurance”. This symptom was also noted in the following cycle. Prover 021 (G.A.), noted from the 10th to the 14th day, a decrease in the hurry and anxiety which characterized his nature, with a kind of mental peace, he wrote “I had the feeling of being less hard in various attitudes, specially with my wife and with those who were closer to me”, this sensation remained for at least 20 days after discontinuing administration of the remedy (O.S.), and this was also associated with an improvement in remembering the names of people. We may observe that mental symptoms were noted only in the case of 200 K.

EYESIGHT and VERTIGO

Most of the Provers, 10 out of 16, who took 30 CH and 200 K, experienced problems focussing objects, and had a feeling of disorientation. Some wrote they had the feeling of being on a boat. The symptom was associated with eyesight disorders and disorientation. 2 Provers, after discontinuation of the remedy, experienced the same disorders when starting administrations again.

HEAD

From the 10th to the 12th day, Prover 017 (G.P.), reported very severe left frontal cephalea which then disappeared on the 16th day. Prover 010 (P.R.) reported moderate cephalea in the front part of the head, from the 8th to the 12th day. Prover 020 (E.D.C.) pointed out frontal cephalea, more towards the left from the 4th to the 8th day, with a state of mental confusion. (O.S.).

MOUTH

Prover 002 (L.G.) complained of a bitter taste in the mouth from the 7th to the 12th day, and dryness of the mucosae with a burning sensation and the desire for refreshing drinks such as lemonade or fresh water. Prover 008 (P.G.) suffered from aphthae in the mouth from the 6th to the 12th day, with a severe burning pain, which disappeared and appeared newly in different areas of the mouth. The most fastidious occurred on the mucosa of the upper lip, to the left (N.S.). Furthermore, Prover 018 (T.T.) reported burning aphthae during the entire research study, which healed and formed again on the mucosa of the mouth, and particularly localized on the tip of the tongue.

BACK

4 Provers reported marked pain in the cervical region, with irradiation of the pain to the occipital area, and heaviness in the whole head from the 10th to the 14th day (O.S.).

ABDOMEN and RECTUM

About 11 Provers out of 16 noted marked abdominal disorders, such as diffused abdominal swelling, diarrhoea with liquid stools, specially after meals, even though particularly irritating foodstuffs had not

been taken 002 (L.G.), 010 (P.G.), 013 (R.G.), etc 2 subjects reported haemorrhoidal symptoms with bright red blood in the stools.

EXTREMITIES (UPPER AND LOWER LIMBS)

Almost all the Provers, those who took 30 CH and those who took 200 K, described a sense of marked heaviness in the lower and upper limbs, with tiredness that limited their daily actions, often associated with articular pain, specially in the hips and the left glenohumeral joint. For example, Prover 006 (R.N.) wrote that from the 5th to the 9th day she felt his arms and legs heavy, as if they were of stone, with a feeling of swelling, even if in the physical check everything appeared normal, furthermore she described a marked heaviness in the left ankle and right hand (4th finger) (N.S.). Prover 013 (R.G.) reported that between the 7th and the 14th day, he had a feeling of heat, heaviness in the feet and restlessness at night when he went to bed .

MALE GENITAL APPARATUS

3 Provers of the male gender, 2 of whom taking 200 K, 017 (G.P) and 021 (G.A.), and one taking 30 CH, 007 (M.S.), reported decreased libido and precocious ejaculation, noted in more than one occasion. Two of them had experienced decreased libido only rarely in their life, but the more serious aspect was the precocious ejaculation that they had never had (N.S.), this symptom disappeared only one month after discontinuing the remedy. Prover 021 (G.A.) stated that precocious ejaculation improved in the 2 months following administration of the remedy (C.S.), while the other two subjects confirmed that the symptoms of decreased libido and precocious ejaculation were noted for at least 40 days after administration of the remedy.

SKIN

Prover 003 (A.A.) referred that one week after administration of remedy 30 CH, he/ experienced a rash with itchy weals (urticaria) which started in the evening after sunset, accompanied by swelling in the concerned location, migrating, accompanied by much itching, and soothed with cold water. Diarrhoea, 2-4 bowel movements a day, relieved the itching symptom. The symptom was present for 4 days.

2 other Provers, 008 (G.P) and 011 (A.F.), noted diffused itching towards the end of the research study (from the 12th to the15th day).

SLEEP

2 Provers, who took 200 K, 006 (R.N.) and 010 (P.R.), reported agitated sleep with restless dreams, from the 7th to the 9th day, which, according to both was unjustified.

CONCLUSIONS

The above trial clearly extends and completes the 8 symptoms that are present in Materia Medica, and makes the use of Titanium metallicum more clear and applicable, adding --- symptoms compared to placebo which had only --- symptoms. The lupus carcinomatous affection symptom, added by Oscar Boericke, was not noted.

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