THERAPEUTICS

L. Milani

HOMEOMESOTHERAPY FOR PAIN MANAGEMENT IN PRIMARY CHRONIC COXARTHROSIS WITH A HOMEOPATHIC INJECTABLE FORMULATION

RESULT OF A COHORT, RANDOMIZED, CONTROLLED CLINICAL TRIAL

SUMMARY

Coxarthrosis is the localization of chronic degenerative arthropathy of the hip joint. It is a frequent, severe and disabling disease with causes that are both anatomical (special conditions of Circulatory System) and mechanical (joint of major movement and which may also be affected by development anomalies).
Clinical symptoms include pain while walking, functional constraints and joint deformity. Pain is due to load but may be also induced by groin palpation (many trigger points) or passive joint mobilization. The functional constraint is progressive and involves extrarotation movements at first, and later thigh extension and flexion. These constraints have negative consequences on walking, causing pain, which leads to limping and muscle spasm, which limits further muscle movement.
Until a few years ago, the pathogenesis of osteoarthrosis was believed to involve only joint cartilage, but we now know that it also involves subchondral bone alteration.
- In order to verify the therapeutic effectiveness of a new magistral homeopathic injectable formulation called *Coxa-compositum ampoules*, a controlled, cohort, randomized clinical trial was carried out. The clinical trial meets the criteria of homogeneity, identifies a primary objective and dimensions the sample in accordance with statistical criteria of reliability.

1) *Coxa-compositum ampoules* Group
66 patients [27 M (41%); 39 F (59%) - average age = 56.2].
10 weekly homeomesotherapeutic sessions for 10 consecutive weeks into the following local acupuncture points GB 30, GB 29, BL 54, GB 27, GB 28, SP 12 and projection points GB 31, ST 31.

2) *Electroacupuncture* Group
63 patients [28 M (44,5%); 35 F (55,5%) - average age = 53.5].
10 weekly sessions of electrostimulated acupuncture for 10 consecutive weeks. Electric contacts: BL 54(+)/GB 29 (-), GB 30 (+)/GB 27 (-), GB 28 (+)/ST 31 (-), SP 12 (+)/GB 31 (-).
Single use nickel-free needles (SH 0.25 x 25 mm GT) electrostimulated for 25 minutes at high frequency (300 Hz) - low variable progressive intensity depending on individual sensitivity.

- **Home therapy: the two Groups have been treated with the magistral formulation called *Arthros compositum drops* (10 drops twice a day 9 a.m., 3 p.m.) x 10 consecutive weeks.**

In particular, while the *Coxa-compositum ampoules* Group had a 5.5 WOMAC Index at T0, the *Electroacupuncture* Group had a 5.1 WOMAC Index. Ten days after the end of the 10th treatment (T2), the WOMAC Index decreased to 2.2 and 3.4 respectively.

- **The WOMAC score in the *Coxa-compositum ampoules* Group is 3.3.**
- **The WOMAC score in the *Electroacupunture* Group is 1.7.**

The results show that Homeomesotherapy in Acupoints with *Coxa-compositum ampoules* is 50% more effective than *Electroacupuncture* at the same points.
-*Coxa-compositum ampoules* can be injected into selected/specific Acupuncture points to successfully treat chronic pain from primary coxarthrosis with no negative side effects. The improvement is progressive from the first to the tenth weekly session. This treatment is well tolerated and can also be used to control acute and secondary coxarthritis pain.

KEY WORDS

COXARTHROSIS, PAIN MANAGEMENT, HOMEOPATHY, HOMOTOXICOLOGY, PHYSIOLOGICAL REGULATING MEDICINE, ACUPUNCTURE.

INTRODUCTION

Coxarthrosis is the localization of chronic degenerative arthropathy of the hip joint. It is a frequent, severe and disabling disease (1-4) with causes that are both anatomical (special conditions of Circulatory System) and mechanical (joint of major movement and which may also be affected by development anomalies).

- **Primary** coxarthrosis can only be caused by dysmetabolic conditions of the joint cartilage; other disorders including functional overload [e.g. obesity (5)], static consequences of *cavus foot*, e.g. *genum valgum* and external rotation of femoral neck (6), or early obliteration of venous trunks may be concomitant and induce worsening.

- **Secondary** coxarthrosis (50% of total cases of coxarthrosis) may have a variety of causes: inflammation, trauma and bone formation alterations. Some sports (7) such as running (8-13), football (14), soccer (15), weight-lifting (16) and certain jobs (17-23) can also lead to secondary coxarthrosis. Recent updates from Medical Literature have shown that other sports may cause coxarthritis (24-27). A recent review on this subject is particularly interesting (28). However, hip dysplasia remains the main and most disabling cause of secondary coxarthrosis. The arthrogenic effect of dysplasia may be detected from an early onset of coxarthrosis and its severe symptoms.

The underlying cause of coxarthrosis can be detected via x-ray: primary coxarthrosis (FIGURE 1), previous injuries followed by macro or microfractures, previous coxarthritis and dysplasias.

-Clinical symptoms include pain while walking, functional constraints and joint deformity. Pain is due to load but may be also induced by groin palpation (*many trigger points*) or passive joint mobilization. The functional constraint is progressive and involves extrarotation movements at first, and later thigh extension and flexion. These constraints have negative consequences on walking, causing pain, which leads to limping and muscle spasm, which limits further muscle movement.

Until a few years ago, the pathogenesis of osteoarthrosis was believed to involve only joint cartilage, but we now know that it also involves subchondral bone alteration (FIGURE 2). The osteoblast and chondrocyte are both involved in the pathogenesis of osteoarthrosis. Inflammation of the joint capsule, rheumatoid arthritis, coxarthritis of muscle origin, coxarthritis of nerve origin (*burning hip*) are all involved in the pathogenesis of coxarthritis, in addition to coxarthrosis. All these diseases induce hip joint pain of different types and severity.

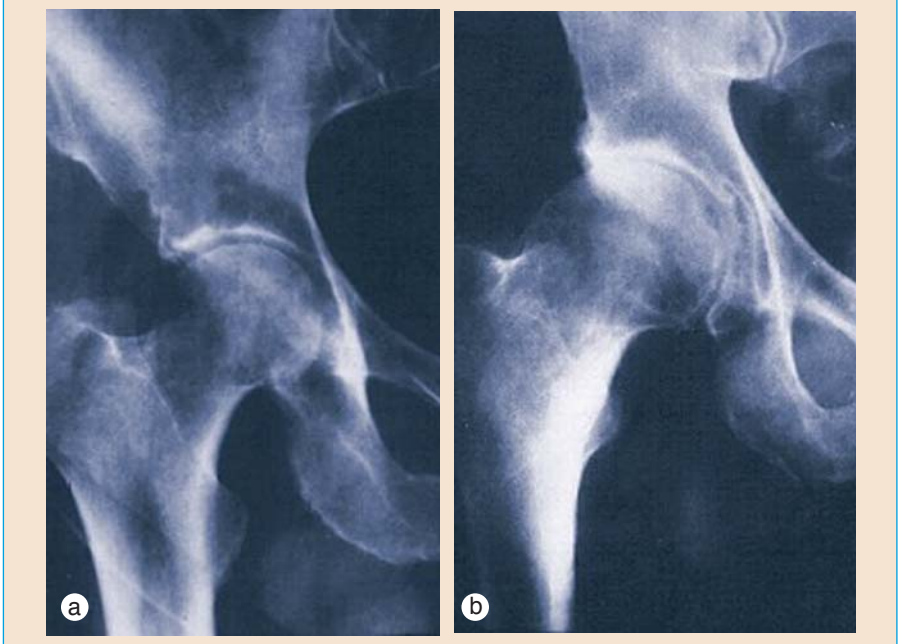


FIGURE 1

a - First-degree primary coxarthrosis. Sclerosis of the articular *tectum* and subchondral cyst. Quite good preserved joint rima;

b - Second-degree primary coxarthrosis: reduction of joint rima; subchondral sclerosis.

FIGURE 2

Columnar alteration and formation of pseudocysts of the subchondral bone in third-degree primary and secondary coxarthrosis.

PHYSIOLOGICAL REGULATING THERAPY (PRT) - THE ITALIAN GROUP

In 1994, an Italian Group of MDs/PhDs (Homeopaths, Homotoxicologists, University Lecturers, Researchers, Allopathic General Practitioners), all members of the Associazione Medica Italiana di Omotossicologia (A.I.O.T. - Milan) and other European specialists agreed to pool their individual professional skills and scientific knowledge to work together on a therapeutic project intended to provide a global, innovative approach to Biological Medicine in the sphere of Traditional Medical Thought. Going beyond the psychosomatic (Classic Homeopathy) and somato-psychic (Homotoxicology) approach, the Italian Group developed a view of the human organism as a **Neuro-Immune-Endocrine Network** regulated by delicate control mechanisms - so-called Physiological Regulating Therapy (PRT).

Over the years, the theoretical and clinical research studies carried out by the Italian Group have led to rational, innovative formulations approved by doctors and patients.
Many recent research projects are focusing on new homeopathic formulations and clinical and experimental projects based on Physiological Regulating Medicine (PRM) (TABLES 1, 2).

MAGISTRAL INJECTABLE FORMULATION *COXA-COMPOSITUM AMPOULES*

Like all the other treatments in the Physiological Regulating Therapy (PRT) range formulated according to the scientific acquisitions on which Physiological Regulating Medicine (PRM) is based, the individual ingredients contained in *Coxa*-compositum ampoules* are selected according to **3 criteria**:

1. Clinical, anatomical and pathological indications for at least 8 out of 10 Homeopathic Materia Medica (H.M.M.) consulted (29-38);
2. A further selection is made to ascertain possible correspondence between classic **homeopathic indications** and **scientific evidence** on the effects of the bio-active substances contained in the selected unitary remedies;
3. Inclusion in the formulation of *cytokines* and *neurotransmitters*, which are concentrated in the **same proportions as in the human body**.

All 10 unitary remedies contained in *Coxa-compositum ampoules* are in X or C dilutions in line with the *low-dose* principle (hormesis).

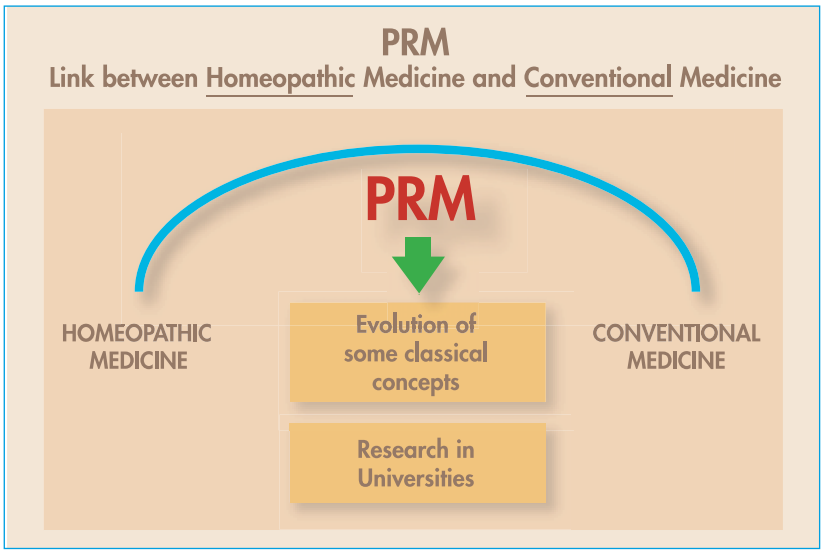
The *low-dose* principle is effectively a subject of current interest and is based on:

1. Arndt-Schultz Law (weak/medium stimuli activate/modulate biological functions);
2. The response of a cell to biological information depends on the *ligand-receptor* effect, so that the response of a cell to a messenger will depend on the number of receptors involved. A typical cell may have approximately 1000 receptors but only a small proportion of them (10%) need to be engaged to obtain a strong response (50%). A surplus of ligands determines a down regulation of membrane receptors (physiological mechanism for maintaining homeostasis): in order to maintain its functional balance, a cell blocks its receptors; this leads at first to delayed reaction and later to loss of function;
3. Bürgi Effect. Different pharmacologically active substances which, when combined, have a synergic effect;
4. *Low-dose* active ingredients can be studied in accordance with Toxicology and Pharmacology, and provide a specific rationale based on the suggestions of the standard Homeopathic Materia Medica and the recent discoveries in such fields as Physiology and Physiopathology (**cytokines**, **neurotransmitters**, **hormones**).

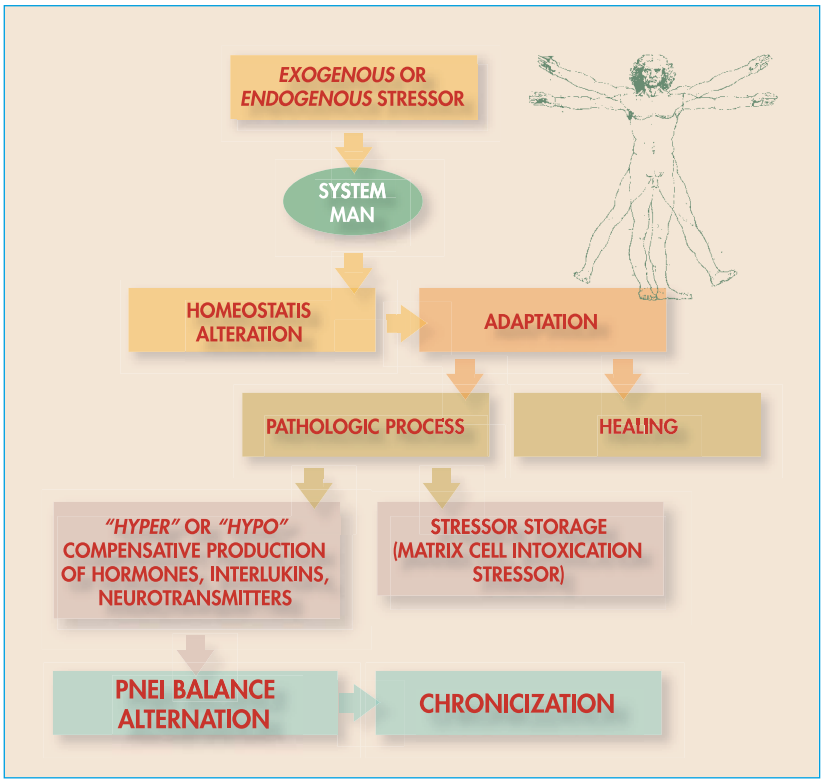
These concepts make it possible to analyze the effect of **each unitary remedy** contained in *Coxa-compositum ampoules* in detail.

- Active ingredients: Arnica montana 8X, **4 parts;** Anti Interleukin 1α 4C, Anti Interleukin 1β 4C, β-Endorphin 4C, Calcarea fluorica 6X; Cartilago-

TAB. 1



TAB. 2



*Derivation of the temporary name = *Coxa* in Latin = hip.

suis 4X, Colocynthis 8X, Rhus toxicodendron 10X, **2 parts**; Argentum metallicum 6X, Formicum acidum 8X, **1 part**.
-Inactive ingredients; sterile isotonic sodium chloride solution.
- 1 ampoule = 2.0 ml.
For a better, more effective understanding of the therapeutic effect of *Coxa-compositum ampoules*, we can select **5 different pharmacological action cores** as follows:

1ST CORE
Homeopathic Antalgic Core

Arnica montana 8X; *Colocynthis* 8X; *Rhus toxicodendron* 10X; *Formicum acidum* 8X; *Argentum metallicum* 6X.
The unitary remedies that are contained in the 1st Core are:
- **Arnica**
(Arnica montana L. - Fam. Compositae).
The bioactive substances are as follows: *helenalin*, which modulates many processes influencing inflammatory reactions, including oxidative phosphorilation, histamine release, serotonin and platelet aggregation, and is also a booster of phagocytosis; *helenin*, *tenuline* and *camixonolid*, which produce the same effect as *helenalin*, although to a lesser extent. *Helenin* is a powerful anti-inflammatory molecule whose mechanism of action is still unknown in spite of all the research studies found in scientific literature. It is the only anti-inflammatory remedy capable of acting both on NF (Necrosis Factor) and I Kappa B. The effect of these bio-substances is enhanced by *caffeic acid* (inhibitor of cyclooxygenase and 5-lipooxygenase - key enzymes for the synthesis of leukotrienes, prostaglandins and hyaluronidase), *arabin 3-6 galactose* (inhibitor of the complement and stimulant TNF macrophage activity), *arnidiol*, *faradiol*, *heteroglycans* (immunomodulating effect).
- According to H.M.M. involving the hip joint: painful hypersensitivity, anti-inflammatory.

- **Colocynthis**
(Cucumis colocynthis L. - Fam. Cucurbitaceae).
The bioactive substances are: *colocynthin*, *cucurbitacin*, *citrullol*, active ingredients acting on rheumatic and nerve diseases and having a cicatrizing action on muscle *trigger points* and lesions of the hip joint capsule.
- According to H.M.M. involving the hip joint: crural pain, genital nerve pain. One of the characteristics of Colocynthis-type nerve pain is spasm and muscle contracture. The patient complains of a sensation of tendon and psoas muscle shortening.

- **Rhus tox.**
(Rhus toxicodendron L. - Fam. Anacardiaceae).
The bioactive substances are: *urushiol*, *toxicodendrol*, *toxicodendrins* having anti-inflammatory and anti-rheumatic properties (subacute and chronic forms).
- According to H.M.M. involving the hip joint: action on tendon pain, diseases affecting ligaments and joints caused by muscle and/or capsule triggers, stiffness (worsening with cold and damp weather), pain on starting movement. Painful stiffness of tendons, ligaments, joints and muscles. Improvement with warmth.

Note: 1 of the 2 Rhus tox. Weihe Points is localized on Acupuncture point GB 30 (*Roann-tiao*), a key point for homeomesotherapeutic hip pain treatment (see "PATIENTS AND METHODS").
- **Formicum acidum**
Promotes the release of *histamine*, *serotonin* and *kallikrein*.
- According to H.M.M. involving the hip joint: joint stiffness worsening with cold and damp weather; sensation of tendon shortening, sharp pain and muscle cramps.

- **Argentum metallicum**
Specifically indicated for fibrous and fibrous-elastic tissues. It affects the joint cartilage, which becomes inflamed, infiltrated and rigid.
- According to H.M.M. involving the hip joint: Argentum treats to chronic deforming rheumatisms and especially to deforming hip joint osteoarthrosis. Hip pain worsening with immobility, cold and damp weather leading to joint cartilage congestion.

GENERAL AND SYNERGIC EFFECTS OF THE UNITARY REMEDIES CONTAINED IN THE **1ST CORE** OF *COXA-COMPOSITUM AMPOULES*: IMPORTANT ANTI-INFLAMMATORY AND ANTI-PAIN EFFECT ACTING ON ALL ANATOMICAL STRUCTURES OF THE HIP JOINT (CAPSULE, TENDONS AND MUSCLES).

2ND CORE
PNEI Antalgic Core

- **β-Endorphin** 4C (FIGURE 3)
This endogenous opioid peptide neurotransmitter found in the neurons of both the Central and Peripheral Nervous System is a peptide - 31 amino acids - resulting from the processing of the precursor POMC - proopiomelanocortin. The highest concentration of endorphin receptors can be found in the gelatinous matter of the spinal cord, periaqueductal gray, thalamus, in all the structures of the limbic brain, all of which are involved in pain recognition, modulation and control. A solid circadian β-Endorphin response rhythm has been proved showing a peak at 12 p.m. and lowest point at 12 a.m. (39). At a physiologi-

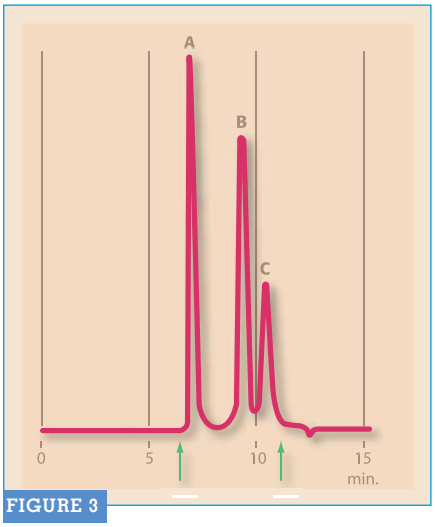


FIGURE 3

A = β - Endorphin;
B = α - Endorphin;
C = γ - Endorphin.
Recording of peak activity after acute pain stimulation.
- The highest Endorphins activity can be recorded from the 7th to the 11th minute, after appropriate stimulation.

cal level, endorphins are secreted in picograms (0.000000000001 g = 10^{-11} g = 11X), 8X on average (= 4C). The β-Endorphin concentration in *Coxa-compositum ampoules* is physiological, similar to the normal concentration within the body. Much evidence has shown that β-Endorphin has an anti-inflammatory effect in addition to relieving pain (39, 40). β-Endorphin can also boost the Immune System and affect mood.

GENERAL EFFECT OF THE UNITARY REMEDY CONTAINED IN THE **2ND CORE** OF *COXA-COMPOSITUM AMPOULES*: ANALGESIC, ANTI-INFLAMMATORY, IMMUNOSTIMULATING ACTION, MOOD IMPROVEMENT (greater response of the patient to the treatment).

3RD CORE

Anti-inflammatory Core

- Anti IL-1α 4C**; Anti IL-1β** 4C (FIGURE 4)

From a biological point of view, interleukins 1 (IL-1α; IL-1β) are the most active inflammation mediators secreted by Th1 cells. They induce inflammation by means of their own capacity to stimulate the genic expression associated with inflammatory process evolution.

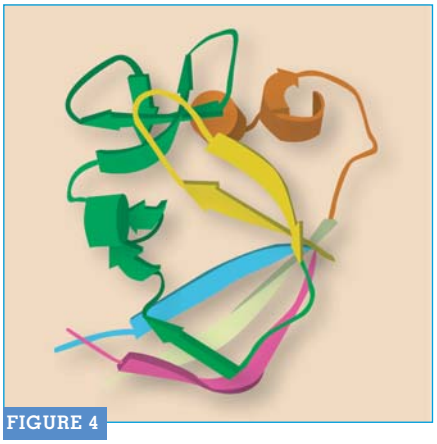


FIGURE 4

Three-dimensional stylized structure of IL 1α.

- Although they may have different structures (coded by 2 different genes), they act on the *same specific receptor*. IL-1 have a very short half-life and are secreted by IL-1 themselves when they encounter CD4 lymphocytes.

IL-1 (α ; β) activate cyclooxygenase type 2 (COX2), prostaglandin E2 and nitric oxide, thus activating the entire inflammatory process (pro-inflammatory Interleukins).

▶ As a consequence, **Anti**-Interleukins 1 (α ; β) act like NSAIDs, cortisone and to some extent like salicylates (41-43), without the negative side effects caused by these allopathic chemical medicines. Homeopathically diluted Anti IL-1α and Anti IL-1β are successfully used in osteoarthrosis and myalgic pain management therapy.

GENERAL AND SYNERGIC EFFECT OF THE UNITARY REMEDIES CONTAINED IN THE **3RD CORE** OF *COXA-COMPOSITUM AMPOULES*: ANTI-INFLAMMATORY ACTION IN BOTH ACUTE AND CHRONIC PHASE.

4TH CORE

Anti-degenerative Core

- Cartilago suis 4X

Homeopathic dilution of the joint cartilage from the knee and hip of young hog hindquarters. Specific organ preparation for the treatment of cartilage injuries, coxarthritis and deforming arthrosis with a trophic and restructuring effect.

- Argentum metallicum

(see 1st Core - Homeopathic Antalgic Core)

GENERAL AND SYNERGIC EFFECT OF THE UNITARY REMEDIES CONTAINED IN THE **4TH CORE** OF *COXA-COMPOSITUM AMPOULES*: TROPHIC AND ANTIDEGENERATIVE EFFECT ON THE JOINT AND PERIARTICULAR STRUCTURES OF THE HIP.

5TH CORE

Constitutional and Trophic Core

- Calcarea fluorica 6X

The amorphous part of the bone is made of calcium phosphate (*Calcarea fluorica*), calcium carbonate and phosphate, magnesium carbonate and phosphate, hydroxyapatite.

When cartilage is affected, the subchondral bone can be subject to thinning and deteriorating processes. At the beginning, this reduction can lead to the formation of osteophytes, a pathological mechanism of joint compensation. Besides being an important constitutional remedy, Calcarea fluorica counterbalances losses and is thus the most appropriate mechanical and functional support to cartilage damage.

- According to H.M.M. involving the hip joint: deforming rheumatisms where joint cartilage and periarticular tissues harden, with potential coxarthrosis leading to ankylosis. Worsening after a period of rest (*Rhus toxicodendron*).

GENERAL AND SYNERGIC EFFECT OF THE UNITARY REMEDY CONTAINED IN THE **5TH CORE** OF *COXA-COMPOSITUM AMPOULES*: TROPHIC, RESTRUCTURING AND ANTI-DEGENERATIVE EFFECT.

From a detailed analysis of the unitary remedies contained in the **5 homeopharmacological cores** of *Coxa-compositum ampoules* we can infer that they have common actions as follows:

1. Synergic
2. Complementary
3. Complete

to treat those diseases for which *Coxa-compositum ampoules* has been formulated (main clinical directions: primary and secondary coxarthrosis, coxarthritis).

▶ According to these considerations, a specific cohort, randomized, controlled clinical trial was carried out to evaluate the therapeutic effect of *Coxa-compositum ampoules* objectively.

PATIENTS AND METHODS

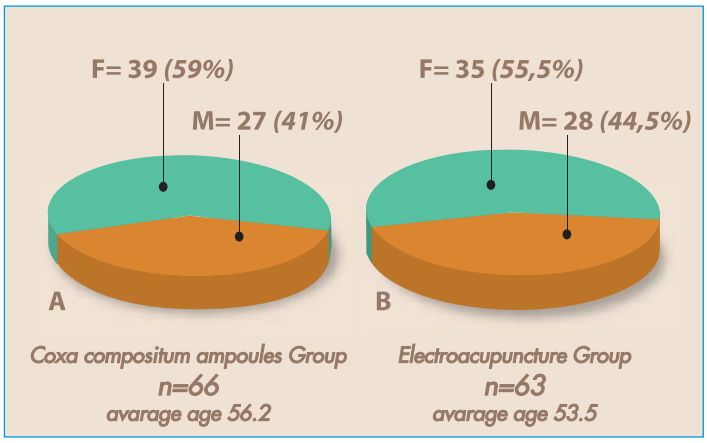
In order to verify the therapeutic effectiveness of *Coxa-compositum ampoules*, a cohort, randomized, controlled clinical trial was carried out. The clinical trial meets the criteria of homogeneity, identifies a primary objective and dimensions the sample in accordance with statistical criteria of reliability.

1) COUNTRY: Italy - 3 Orthopaedic and Rheumatology Clinics
2) NUMBER OF PATIENTS RECRUITED: 129 [55 M (43%); 74 F (57%)]
3) PATIENTS' AGE: average 54.8 year old - Min: 42.3; Max: 68.5
4) TRIAL PERIOD: September 2002 - June 2005
5) PATHOLOGY:
Coxalgia caused by 1st and 2nd degree primary coxarthrosis acc. to Hubbard
6) INCLUSION CRITERIA:
   a) Primary coxarthrosis clinically evidenced and diagnosed on the basis of algic symptoms of the hip joint reported by the patient
   b) 1st and 2nd degree coxarthrosis (X rays)
   c) Enduring pain for at least 4 months without signs of acute inflammation
7) EXCLUSION CRITERIA:
   a) Secondary coxarthrosis
   b) Relapsing coxarthrosis
   c) Patients previously treated with costicosteroids during the 6 months prior to recruitment
   d) Slight pain
8) RECRUITING CRITERIA:
Random, according to the patient's recruitment time
9) TREATMENT:

A) *Coxa-compositum ampoules* Group
- **66 patients** [27 M (41%); 39 F (59%) - average age = 56.2] (TAB. 3)

10 weekly homeomesotherapeutic sessions for 10 consecutive weeks into the following local acupuncture points GB 30, GB 29, BL 54, GB 27, GB 28, SP 12 and projection points GB 31, ST 31 (FIGURE 5). The local and projection points for the infiltration of *Coxa-compositum ampoules* were selected according to the clinical indication of 8 out of 10 reference Acupuncture textbooks consulted (44-53) and on the basis of the experience of the managers at the 3 Pain Clinics where the trial was carried out.

Each local point was treated by making an intradermic injection (FIGURE 6) with 0.5 ml; except for acupoint GB30, where the medicine was injected at a depth of 2 cm.
Syringe: 5cc; needle 13 mm - 30 G.
Into GB 30: intramuscular injection needle (4 cm).
- Home therapy: magistral formulation called *Arthros compositum drops* ** (10 drops twice a day at 9 a.m. and 3 p.m.) x 10 consecutive weeks.



TAB. 3
The two Groups are homogeneous regarding disease, degree of pathology, number, sex and average age distribution.

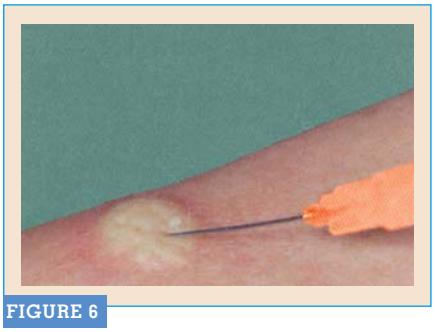


FIGURE 6
Formation of a wheal during intradermic infiltration.

B) *Electroacupuncture* Group
- **63 patients** [28 M (44,5%); 35 F (55,5%) - average age = 53.5] (TAB. 3).

10 weekly sessions of electrostimulated acupuncture for 10 consecutive weeks.
Electric contacts: BL 54(+)/GB 29 (-), GB 30 (+)/GB 27 (-), GB 28 (+)/ST 31 (-), SP 12 (+)/GB 31 (-).
Single use nickel-free needles (SH 0.25 x 25 mm GT) electrostimulated for 25 minutes at high frequency (300 Hz) - low variable progressive intensity depending on individual sensitivity.

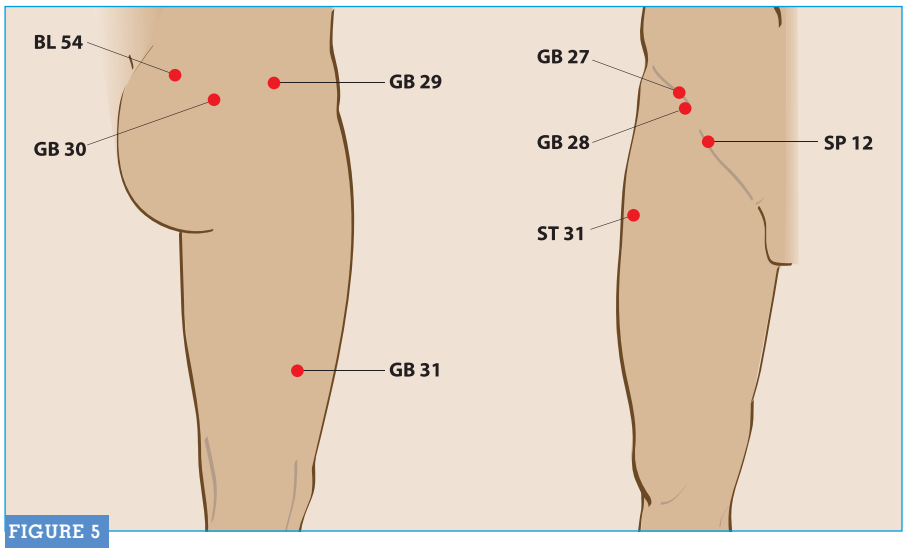


FIGURE 5
Acupuncture Points infiltrated with *Coxa-compositum ampoules* (*Coxa-compositum ampoules* Group) or *Electroacupuncture* (*Electroacupuncture* Group).

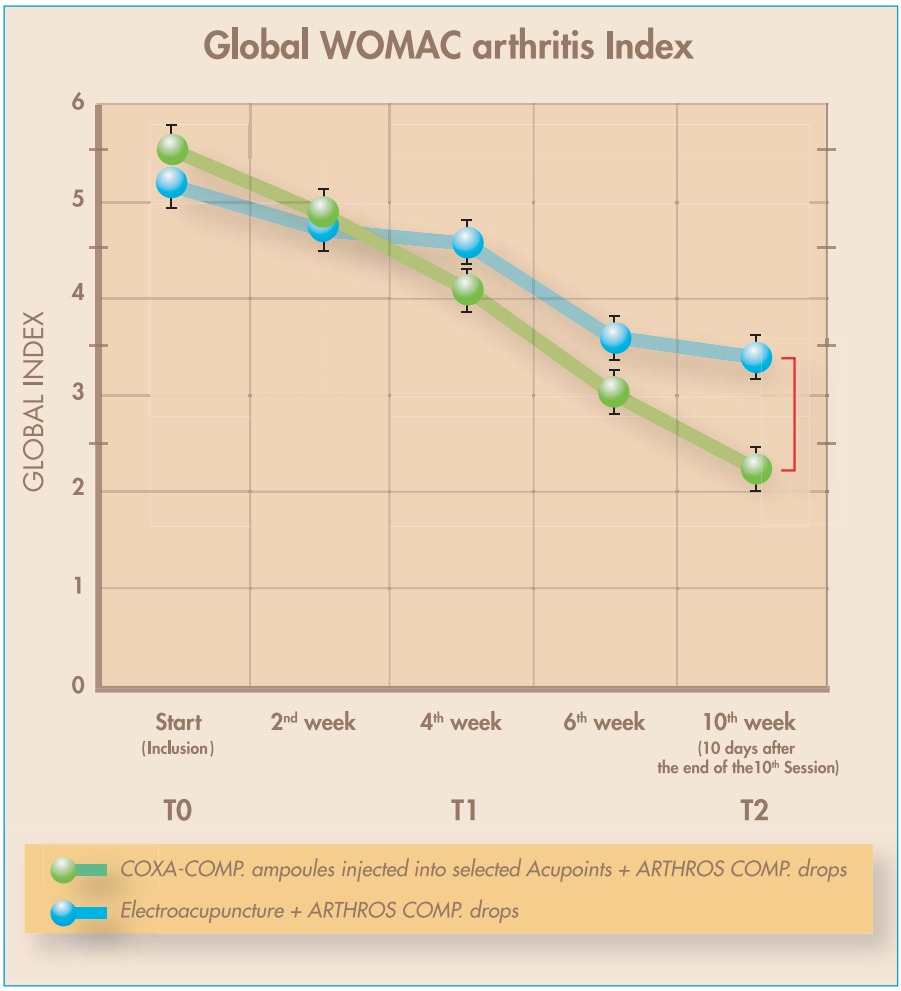
** ***Arthros compositum drops*** = Ascorbic ac. 2X, Sulphur 3X, Chlorinum 6X, Nadidium 3X, Na oxalaceticum 3X, α-Ketoglutaricum ac. 3X, α-Lipoicum ac. 3X, Barium oxalsuccinate 3X (**Metabolic core**); Artery, Porc. 6X, Vein, Porc. 6X, Cartilago suis 6X, Placenta totalis suis 6X, Funiculus umb. suis 6X, Sulphur 3X, FGF 4C, NGF 4C (**Trophic core**); Parathyroid Gl., Porc. 6X, Calcitonin 6X (**P.N.E.I. core**); Bryonia 6/8/12X, Cimicifuga 6/8/12X, Dulcamara 6/8/12X, Rhus tox. 6/8/12X (**Anti-inflammatory core**); Gland. suprarenalis suis 6X, Colchicum 6/8/12X, Strontium carbonicum 6/8/12X (**Antidegenerative core**).

- Home therapy: magistral formulation called *Arthros compositum drops* (10 drops twice a day 9 a.m., 3 p.m.) x 10 consecutive weeks.

RESTRICTIVE TRIAL CRITERIA

- We chose **not** to compare the *Coxa-compositum ampoules* Group vs. a Group treated with local infiltrations of injectable NSAIDs because the latter, according to precise indications from the producers, can be infiltrated neither i.d. nor s.c.
- We chose **not** to compare the *Coxa-compositum ampoules* Group vs. a Group treated with local anaesthetics because the latter are potentially dangerous (individual hypersensitivity, anaphylactic reaction, or shock).
- We chose **not** to compare the *Coxa-compositum ampoules* vs. a Group treated with placebo local infiltrations because it is not ethically correct according to the *"Declaration of Helsinki"* (1st section: October 2001; 2nd section: March 2003) and not patient-oriented.

All patients signed the mandatory form giving their informed consent, with specified declaration that both injectable ampoules and drops were *magistral formulations* that would not cause negative side effects, because the X or C dilutions of the single ingredients were much higher than the minimum toxic dose.



TAB. 4

The two Groups had the same WOMAC Index at T0 (clinical homogeneity): 5.5 for the *Coxa-compositum ampoules* Group and 5.1 for the *Electroacupuncture* Group respectively. The differences between the two Groups began from the 2nd week of treatment (after the 3rd session) and became evident starting from the 6th week of treatment (after the 7th session). In the *Electroacupuncture* Group the WOMAC Index at the 7th session was 3.5, while it was 3.4 10 days after the end of the 10th session. In the *Coxa-compositum ampoules* Group the WOMAC Index was 3.0 at the 7th session, while it was 2.2 10 days after the end of the 10th session.

EVALUATION CRITERIA *(OUTCOMES)*

PATIENTS

All patients included were evaluated according to:

A) **WOMAC** - Osteoarthritis Index Questionnaire (Western Ontario and Mac Master Universities). Since its development in 1982, the WOMAC Index has undergone many revisions and modifications. The WOMAC Index is self-administrated and assesses the amplitudes of pain, disability and joint stiffness *(www.auscan.org/womac/index.htm)*.
The WOMAC Index Questionnaire is designed to evaluate patients' conditions according to 3 criteria:
1) Pain (5 items: walking, walking up stairs, walking down stairs, at rest, during the night) at T0 (inclusion), T1 (after 5 sessions), T2 (10 days after the end of the 10th session). Each item is scored on a scale from 0 (no pain/problem) to 10 (worst pain/foreseeable problem);
2) Stiffness (2 items: in the morning, during the day);
3) Physical functionality (7 items - e.g.: to bend over, to put on socks or stockings, to stand, etc.);

B) **SF-36 Questionnaire** - the most widespread and best-known patient-oriented questionnaire about the general health status - 9 items - among which: vitality, social functioning, physical functioning, general health (at T0 and T2).

DOCTORS

Clinical evaluation (hip extrarotation, thigh extension, bending of the thigh on the pelvis, evaluation of the ability to walk on a flat floor).

THERAPEUTIC EFFECTIVENESS

See TAB. 4

PATIENT COMPLIANCE

- *Coxa-compositum ampoules* Group: very good+ good = 90%
- *Electroacupuncture* Group: very good+ good = 82%

TOLERANCE

- In both groups: very good + good = 96% (±1)

FINAL RESULT

Statistically significative superiority of *Coxa-compositum ampoules* vs. *Electroacupuncture* in the same points.

CONCLUSIONS

By comparing the effectiveness of Homeomesotherapy with *Coxa-compositum ampoules* vs. *Electroacupuncture*, the two treatments were shown to be effective in reducing chronic pain from primary coxarthrosis with a **greater** and **more rapid** statistically significant improvement for the patients in the *Coxa-compositum ampoules* Group (exact Fisher test $p < 0.01$).

In particular, while the *Coxa-compositum ampoules* Group had a **5.5** WOMAC Index at T0, the *Electroacupuncture* Group had a **5.1** WOMAC Index. Ten days after the end of the 10th session, the WOMAC Index decreased to **2.2** and **3.4** respectively.

- The WOMAC score in the *Coxa-compositum ampoules* Group is **3.3** (TAB. 4)
- The WOMAC score in the *Electroacupunture* Group is **1.7**

Frontal view of an electrodermic point:
A - with positive stimulus
B - with negative stimulus
C - surface expansion of an electrodermic point
(*apud* Dumitrescu, 1992).

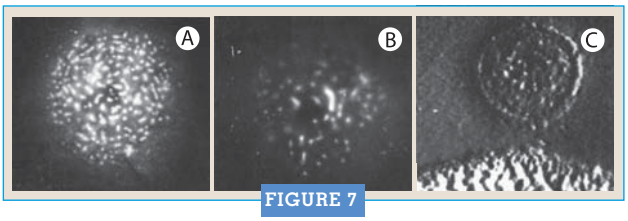
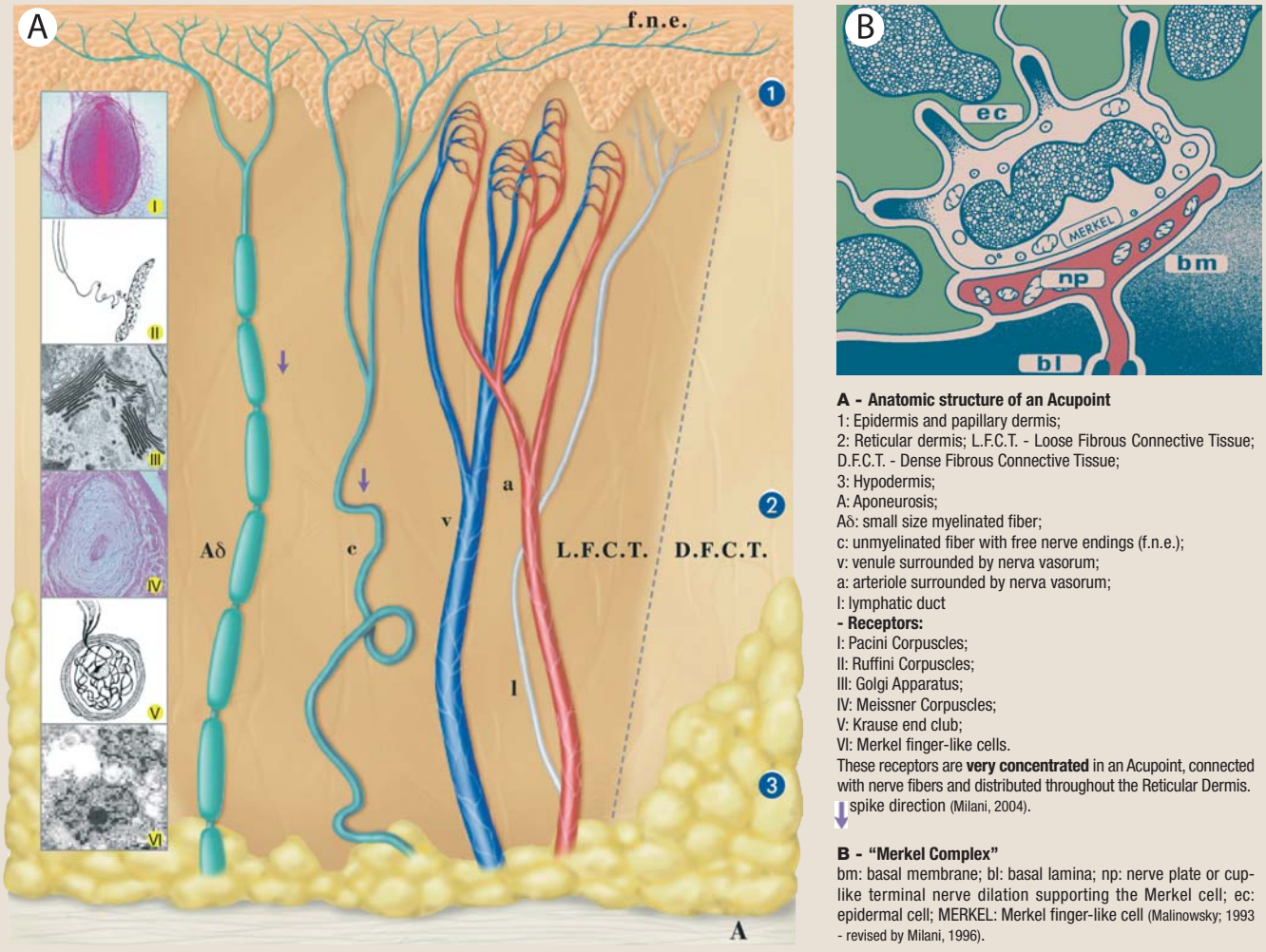


FIGURE 7

FIGURE 8



A - Anatomic structure of an Acupoint
1: Epidermis and papillary dermis;
2: Reticular dermis; L.F.C.T. - Loose Fibrous Connective Tissue; D.F.C.T. - Dense Fibrous Connective Tissue;
3: Hypodermis;
A: Aponeurosis;
Aδ: small size myelinated fiber;
c: unmyelinated fiber with free nerve endings (f.n.e.);
v: venule surrounded by nerva vasorum;
a: arteriole surrounded by nerva vasorum;
l: lymphatic duct
- Receptors:
I: Pacini Corpuscles;
II: Ruffini Corpuscles;
III: Golgi Apparatus;
IV: Meissner Corpuscles;
V: Krause end club;
VI: Merkel finger-like cells.
These receptors are **very concentrated** in an Acupoint, connected with nerve fibers and distributed throughout the Reticular Dermis.
↓ spike direction (Milani, 2004).

B - "Merkel Complex"
bm: basal membrane; bl: basal lamina; np: nerve plate or cup-like terminal nerve dilation supporting the Merkel cell; ec: epidermal cell; MERKEL: Merkel finger-like cell (Malinowsky; 1993 - revised by Milani, 1996).

The results show that Homeomesotherapy in Acupoints with *Coxa-compositum ampoules* is **much more effective** than *Electroacupuncture* at the same points (WOMAC Global Index scores difference: **1.6**). As the local treatment was accompanied by the same home treatment for both Groups (*Arthros-compositum drops*), the differences between the 2 Groups' results remain well-grounded and significant. Infiltration into the Acupuncture points with a complex PRT homeopathic medicine is particularly interesting as the same point can benefit from homeopharmacological action and mechanical stimulation. Besides the energetic value of Traditional Chinese Medicine (FIGURE 7), the Acupuncture point has specific anatomical (high receptor density, presence of Merkel cells, presence of myelinated Aδ and non-myelinated c nervous fibers) and physiological characteristics (higher electrical conductivity, different temperature) (FIGURE 8).

- The selected Acupuncture points are localized on dermatomers from T12 to S2, the same nerves innervating the joint capsule, the ligaments, the tendons and the muscles forming the mechanism of the hip joint retention. Another advantage of Homeomesotherapy vs. Electroacupuncture is the time required to perform a single treatment: 5-6 minutes vs. 25 minutes, and the fact that it can be carried out even when the patient is confined to bed, using simple, portable equipment.

▶ On the basis of the above, we can state that *Coxa-compositum ampoules* can be injected into specific, selected Acupuncture points to successfully treat chronic pain from primary coxarthrosis with no negative side effects; the improvement is progressive from the 1st to the 10th weekly session.

This treatment is well tolerated and can also be used to control acute and secondary coxarthritis pain. ■

N.B. The magistral homeopathic formulations *Coxa-compositum ampoules* and *Arthros compositum drops* mentioned in this article have been registered in USA as **GUNA®-HIP** and **GUNA-ARTHRO** respectively.

- **GUNA®-HIP** clinical indications: hip joint osteoarthrosis, hip joint capsule inflammation, hip joint rheumatoid arthritis, hip joint pain of muscle origin, hip joint pain of nerve origin, knee osteoarthrosis.
- **GUNA-ARTHRO** clinical indications: arthrosis, arthritis, muscle pain, articular discomfort.

References

1. Radin E.L. - Aetiology of osteoarthritis. Clin Rheum Dis **1976**; 2: 509-522.
2. Danielsson L., Lindberg H., Nilsson B. - Prevalence of coxarthrosis. Clin Orthop **1984**; 191:110-115.
3. Kelsey J. - Epidemiology of musculoskeletal disorders. Monographs in epidemiology and biostatistics. Oxford: Oxford University Press; **1982**.
4. Typpo T. - Osteoarthritis of the hip: radiological findings and etiology. Ann Chir Gynaecol, **1985**; 74: 5-38.
5. Olsen O., Vingård E., Köster M., Alfredsson L. - Etiologic fraction for physical work load, sports and overweight in the occurrence of coxarthrosis. Scand J Work Environ Health, **1994**;20: 184-188.
6. Bourdiol R.J. - Pied et Statique. Maisonneuve, **1980** *(French)*.
7. Vingård E., Alfredson L., Goldie I., Hogstedt C. - Sports and osteoarthrosis of the hip. Am J Sports Med, **1993**; 21: 195-200.
8. Videman T. - The effect of running on osteoarthritic joint: an experimental matched-pair study with rabbits. Rheumatology and Rehabilitation, **1982**; 21: 1-8.
9. Marti B., Knobloch M., Tschopp A., Jucker A., Howald H. - Is excessive running predictive of degenerative hip disease? Controlled study of former elite athletes. BMJ, **1989**; 299: 91-93.
10. Puranen J., Ala-Keltola L., Peltokallio P., Saarela J. - Running and primary osteoarthrosis of the hip. BMJ, **1975**; 285: 424-425.
11. Lane N.E., Bloch D.A., Wood P.D., Fries J.F. - Aging, long-distance running and the development of musculoskeletal disability. Am J Med, **1987**; 82: 772-780.
12. Panush R.S., Schmidt C. et Al. - Is running associated with degenerative joint disease. JAMA, **1986**; 255: 1152-1154.
13. Sohn R.S., Lyle M.J. - The effect of running on the pathogenesis of osteoarthritis of the hips and knees. Clin Orthop, **1987**; 198:106-109.
14. Klünder K.B., Rud B., Hansen J. - Osteoarthritis of the hip and knee joint in retired football players. Acta Orthop Scand, **1980**; 51: 925-927.
15. Lindberg H., Roos H., Gärdsell P. - Prevalence of coxarthrosis in former soccer players. Acta Orthop Scand, **1993**; 64:165-167.
16. Kujala U., Kaprio J., Srna S. - Osteoarthritis of weight bearing joints of lower limbs in former elite male athletes. BMJ, **1994**; 308: 231-234.
17. Anderson J.A.D. - Arthrosis and its relation to work. Scand J Work Environ Health, **1984**; 10: 429-433.
18. Axmacher B., Lindberg H. - Coxarthrosis in farmers. Clin Orthop, **1993**; 287: 82-86.
19. Vingård E., Alfredsson L., Goldie I., Hogstedt C. - Occupation and osteoarthrosis of the hip and knee. Int J Epidemiol, **1991**; 20: 1025-1031.
20. Croft P., Coggon D., Cruddas M., Cooper C. - Osteoarthritis of the hip: an occupational disease in farmers. BMJ, **1992**; 304: 1269-1272.
21. Croft P., Cooper C., Wickham C., Coggon D. - Osteoarthritis of the hip and occupational activity. Scand J Work Environ Health, **1992**; 18: 59-63.
22. Vingård E., Alfredsson L., Fellenius E., Goldie I., Hogstedt C., Köster M. - Coxarthrosis and physical load from occupation. Scand J Work Environ Health, **1991**; 17: 104-109.
23. Andersson S., Hessel T., Norén A., Nilsson B., Saraste M., Rydholm D. - Degenerative joint disease in ballet dancers. Clin Orthop, **1989**; 238: 233-236.
24. Schmitt H., Hansmann H.J., Brocai D.R., Loew M. - Long term changes of the throwing arm of former elite javelin throwers. Int J Sports Med, **2001**; 22(4): 275-279.
25. Schmitt H., Lemke J.M., Brocai D.R., Parsch D. - Degenerative changes in the ankle in former elite high jumpers. Clin J Sports Med, **2003**; 13(1): 6-10.
26. L'Hermette M., Polle G., Tourny-Chollet C., Dujardin F. - Hip passive range of motion and frequency of radiographic hip osteoarthritis in former elite handball athletes. Br J Sports Med, **2006**; 40(1): 45-49.
27. Gross P., Marti B. - Risk of degenerative ankle joint disease in volleyball players: study of former elite athletes. Int J Sports Med, **1999**; 20(1): 58-63.
28. Martin J.A., Brown T., Heiner A., Buckwalter J.A. - Post-traumatic osteoarthritis: The role of accelerated chondrocyte senescence. Biorheology, **2004**; 41: 479-491.
29. Allen T.M. - The Encylopedia of Pure Materia Medica (12 Voll.). B. Jain. Publisher, New Delhi; **1976**.
30. Binet C. - L'Homéopathie pratique. Dangles Ed., St. Jean de Braye; **1972** *(French)*.
31. Boericke W. - Materia Medica Omeopatica. ISBN 1 - 902575 - 02 - 04 *(Italian)*.
32. Charette G. - La Metière Medicale Pratique. Ed. Médicales, Paris; **1928** *(French)*.
33. Clarke J.H. - Dizionario di farmacologia omeopatica clinica. Nuova IPSA Ed., Palermo; **1987** *(Italian)*.
34. Duprat H. - Materia Medica Omeopatica. F.lli Palombi Ed., Roma; ISBN 88 - 7621 - 000 - 8 *(Italian)*.
35. Hodiamont G. - Trattato di Farmacologia Omeopatica - Piante medicinali in Omeopatia (5 Voll.) - Nuova IPSA Ed., Palermo; **1987** *(Italian)*.
36. Jouanny J. - Matière Médicale Homeopathique. Ed. Boiron, Lyon; **1976** *(French)*.
37. Reckeweg H.H. - Materia Medica Omeopatica. Guna Ed., Milano; **1990** *(Italian)*.
38. Zissu R., Guillaume M. - Manuel de Médicine Homéopathique. Doin Ed., Paris; **1973** *(French)*.
39. Gironi M. et Al. - J. Neural Neurosurg Psychiatry. **2003**; 74: 495-497.
40. Rassmussen N.A., Farr L.A. - Effects of morphine and time of day on pain and β-endorphin. Biol. Res. Nurs., **2003** Oct; 5(2): 105-116.
41. Dinarello C.A. - Biology of interleukin 1. FASEB J. **1988**; 2(2):108-15.
42. Dinarello C.A. - The IL-1 family and inflammatory diseases. Clin Exp Rheumatol., **2002**; 20(5 Suppl 27):S1-13.
43. Oppenheim J.J. - There is more than one interleukin 1. Immunol. Today, **1986**; 7: 45-56.

44. An Outline of Chinese Acupuncture. The Academy of Traditional Chinese Medicine. Foreign Languages Press, Peking; **1975**.
45. Bischko J. - An introduction to Acupuncture. Haug Verlag, Heidelberg; **1978**.
46. Bonnet-Lemaire M. - Acupuncture chinoise appliqué - Règles du choix des points. Librairie Maloine Edit., Paris; **1940** *(French)*.
47. Bossy J., Maurel J.C. - Acupuncture. Masson Ed., Paris; **1976** *(French)*.
48. Ferreyrolles P. - Acupuncture chinoise. Ed. S.L.E.L., Lille; **1953** *(French)*.
49. Milani L. - Agopuntura sconosciuta e nuova. Ed. Libreria Cortina, Milano; **1980** *(Italian)*.
50. Niboyet G. - Essai sur l'acupuncture chinoise pratique. Ed. Wayle, London; **1951** *(French)*.
51. Voisin H. - Agopuntura Cinese. DEMI Ed., Roma; **1973** *(Italian)*.
52. Yu-Lin Lian et Al. - Atlante Seirin di Agopuntura. Per l'edizione italiana: Könemann Verlagsgesellschaft; **2001** *(Italian)*.
53. Zhang Rui F. - I punti di Agopuntura e i loro meccanismi d'azione. Masson Ed., Milano; **1994** *(Italian)*.

The following articles and textbooks were also consulted:

1. Dumitrescu F. - Acupuncture scientifique moderne. Progres et perspectives. Tecnique et Documentation. Lavoisier, Paris; **1986**.
2. Lewith G.T., Machin D. - On the evaluation of the clinical effects of acupuncture. Pain, **1983**, 16; 111-127.
3. Yamamura Y., Tabosa A., Cricenti S.V., Di Dio L.J.A. - Spinal nerves and acupuncture. Rev. Assoc. Med. Bras, **1995**; 42: 115-118.
4. Milani L., Roccia L. - L'importanza del metamero nell'interpretazione dei risultati terapeutici ottenuti con agopuntura - Minerva Medica. Vol. 82; 3735-3741; **1980** *(Summary in English)*.
5. Milani L. - Agopuntura come embrio-riflessoterapia: una nuova teoria. Minerva Medica, **1983**; Vol. 74; 2547-2556 *(Summary in English)*.
6. Milani L. - (Coordinator of the International Advisory Committee) - Homeopathy: the scientific proofs of efficacy. Guna Ed., Milano; **2002**.
7. Milani L. - Omeosiniatria e trigger miofasciali: un'accoppiata vincente. Prima parte. La Med. Biol. **2003**/2; 31-41 *(Summary in English)*.
8. Milani L. - Weihe e altri Punti. Tra Agopuntura e Omeopatia. Libro-Atlante. Guna Ed., Milano; **2004**.
9. Riley D., Jütte R. - A review of the use and role of low potencies in homeopathy. Complementary Therapies in Medicine, **2006**.

Author's address

Prof. Leonello Milani
- A.I.O.T. Vice President
- Scientific Director of "La Medicina Biologica"
- Professor "Honoris Causa" of Istituto Superiore Studi Sanitari, Rome (Centre cooperating with W.H.O.)

Via G. Washington, 98
20146 Milano - Italy