Research Article ISSN 2769-6294

International Journal of Biomedical Research & Practice

Bone Disease and New Prevention Frontiers Chapter One: Osteoporosis

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Received: 10 Feb 2022; **Accepted:** 12 Mar 2022; **Published:** 16 Mar 2022

Citation: Riccardi B, Resta S. Bone Disease and New Prevention Frontiers Chapter One: Osteoporosis. Int J Biomed Res Prac. 2022; 2(1); 1-11.

ABSTRACT

In this first chapter, we describe different Osteopathies of degenerative or inflammatory nature related to the ageing of people. We are going to give a brief description of the pathogenic processes responsible for bone diseases, with a particular focus on osteoporosis and we will present various options and proposals for the prevention and treatment of changes in bone metabolism with medicines and food supplements. We are going to devote particular attention to the effects of Silicon in these pathologies, until now poorly considered, and we will propose our own formulation composed of Organic Silicon plus trace elements. We have treated a large number of patients, osteopenics or osteoporotics and we have obtained good and encouraging results with this innovative formulation. We therefore consider the proposal presented here to be a valid alternative to traditional pharmacological treatment, with respect to which it has the double advantage of equal effectiveness and absolute absence of side effects.

Keywords

Osteoporosis, Osteopenia, Food supplements, Patented Organic Silicon G5, Trace elements.

Introduction

From Healthy Bone to Pathological one

Skeleton Structure and composition: Our skeleton is made up of bone and cartilage. The bone is a complex structure formed by an organic component of dense connective tissue, which represents the substrate, the scaffolding on which the inorganic mineral component formed by different salts is deposited. The nourishment of the bones is provided by blood and lymphatic vessels while the nerve fibers allow the passage of sensitive stimuli.

Functional homeostasis is ensured by some specialized cells dispersed in the mineral component, with their activity they ensure the continuous synergy remodeling of the bone in response to environmental stimuli and mechanical stresses Figure 1. Therefore, the elasticity is due to the organic component and the resistance due to the inorganic component. A translucent elastic substance forms the cartilage component that covers the joint surfaces to facilitate the sliding and absorb the mechanical stresses of the bone segments. A fundamental substance, cells and fibers form cartilage.

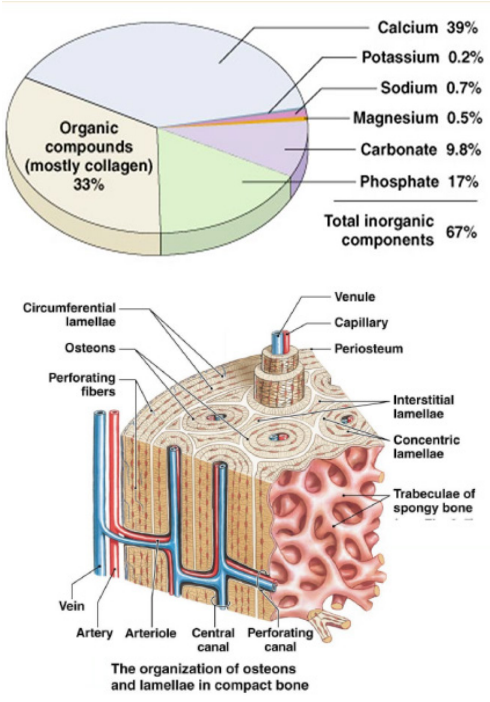


Figure 1: Bone structure and chemical composition (From our file).

The functional task of the skeleton is in order to provide mechanical support to the muscles for the functioning of static and dynamic activity during the rest and movement of vertebrates, and also to contain and to protect the tissues and vital organs of our body, brain in the braincase, heart and lungs in the thoracic cage, digestive tract and urinary tract in the pelvis. Another fundamental functional aspect of bone tissue is to provide a reserve of minerals essential for maintaining the homeostasis of bone minerals and other tissues. Also essential is the role that the bone marrow plays in the hematopoiesis of the blood cells and the immune system.

Bone organic matrix (ECM bone) and connective tissue

The organic component of bone is formed by connective tissue, a specialized tissue also present in different systems and organs.

The ECM (Extra Cellular Matrix) is a non-cellular three-dimensional structure secreted by cells into the extracellular space. It is composed of specific proteins and polysaccharides. The bone matrix comprises organic (40%) and inorganic compounds (60%). Moreover, its exact composition differs based on sex, age, and health conditions. The main inorganic components of the ECM are calcium-deficient apatite and trace elements. By contrast, the organic ECM is significantly more complex consists mainly of collagen type I (90%), and non-collagenous proteins (10%). Bone ECM dynamically interacts with osteoblast-lineage cells and osteoclasts to regulate the formation of new bone during regeneration Figure 2 [1-2].

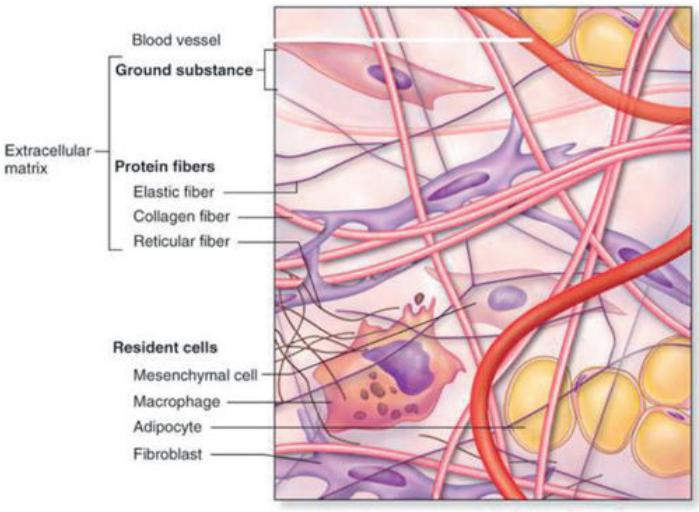


Figure 2: Extracellular matrix and connective tissue of the bone, from Dwi Liliek Kusindarta and Hevi Wihadmadyatami; Role of Extracellular Matrix in Tissue Regeneration http://dx.doi.org/10.5772/intechopen.75728.

The connective is particularly suitable to form the scaffolding supporting all tissues of our body. It derives from the embryonic mesenchima sheet differentiated and specialized during the development of the embryo, giving rise to the support network of the extracellular matrix of tissues. Performs important functions: connection of other tissues, mechanical, trophic, defensive. Connective tissues consist of cells, extracellular matrix, fibers. The fundamental substance is composed of Glycosaminoglycans (GAGs), Proteoglycans, Fibronectin and Glycoproteins [3]. Connective cells are represented by fibroblasts, macrophages, melanocytes, mast cells, granulocytes, etc. The fibers are collagen fibers and elastic fibers.

Collagen plays a role of primary importance, because it is the basic building block supporting organs and organic systems. Collagen has a filamentous structure organized into bundles that form a triple helix structure; the smallest constituents are formed by the Tropocollagen Figure 3.

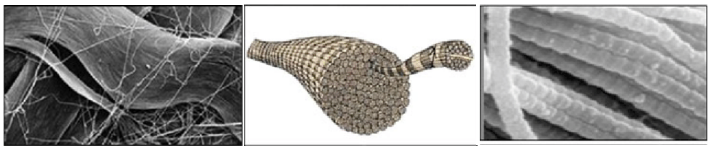


Figure 3: Intimate structure of Collagen (From our file).

The triple helix of collagen is made compact and stable by a particular sequence of amino acids: glycine, proline or hydroxyproline. Below is shown a typical structure of collagen Figure 4.

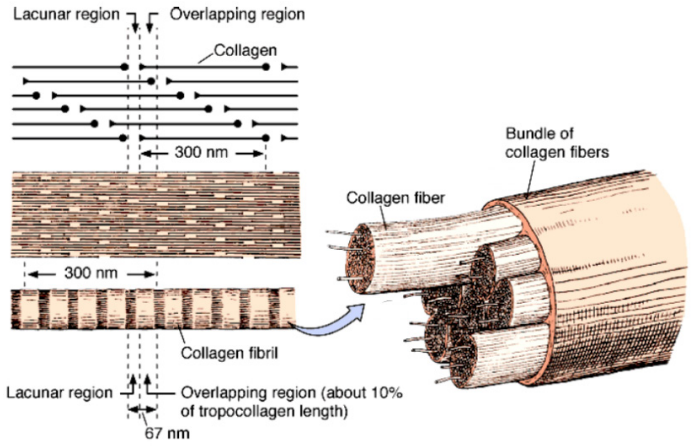


Figure 4: Collagen structure, From the Structure and Function of Collagen, https://owlcation.com/stem/The-Structure-and-Function-of-Collagen

Elastic fibres Elastin

Elastin is the major component of elastic fibres. It is an extremely hydrophobic protein, about 750 amino acids long, it is rich in proline and glycine as collagen but, unlike collagen, it is not glycosate and contains many residues of hydroxyproline and not hydroxysilysine.

Glucosaminoglycans (GAGS) and proteoglycans (PGs) form within the connective tissues a substance called "fundamental" highly hydrated gelatinous, within which fibrillar proteins are embryonic. The gelatinous polysaccharide substance is capable, on the one hand, of enabling the ECM to resist considerable compressive forces and, on the other hand, of allowing a rapid and constant diffusion of nutrients, metabolites and hormones between blood and tissues.

Below is the collagen synthesis, where all the essential steps are summarized Figure 5 [4].

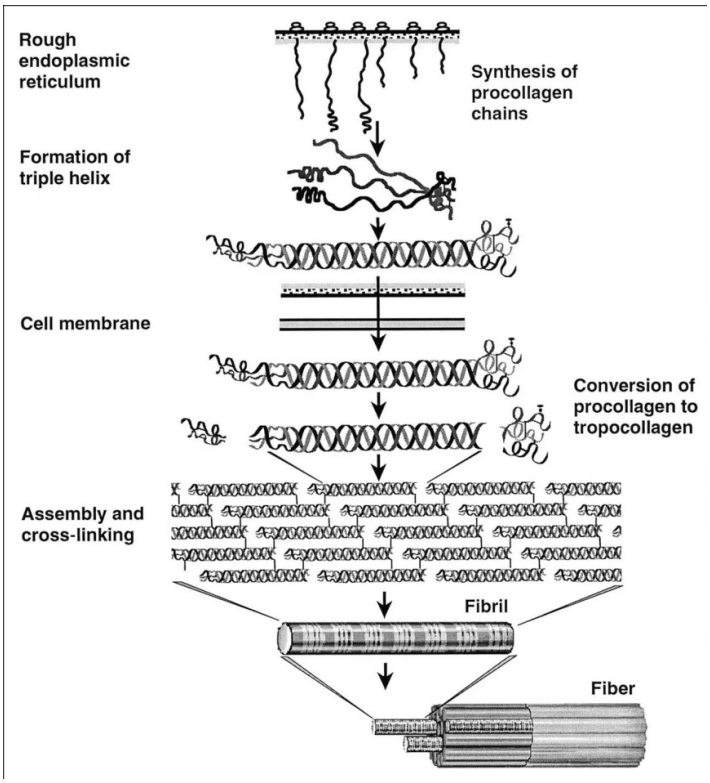


Figure 5: Fundamental stages in the synthesis of collagen, From the Structure and Function of Collagen, from: https://owlcation.com/stem/The-Structure-and-Function-of-Collagen

Bone cells

The fundamental cellular elements of the bone that govern the remodeling and neoformation of the bone (Osteogenesis) are:

- Osteoblasts, synthesize matrix,
- Osteocytes, mature bone cells, derived from osteoblasts, trapped in gaps,
- Osteoclasts, multinational, derived from macrophages-granulocytes, act in reabsorption.

Osteogenesis

The terms osteogenesis and ossification are often used synonymously to indicate the process of bone formation. Parts of the skeleton form during the first few weeks after conception. By the end of the eighth week after conception, the skeletal pattern is formed in cartilage and connective tissue membranes and ossification begins. Bone development continues throughout adulthood. Even in adult is attained, bone development continues for repair of fractures and for remodeling to meet changing lifestyles. Osteoblasts, osteocytes and osteoclasts are the three cell types involved in the development, growth and remodeling of bones. Osteoblasts are bone-forming cells; osteocytes are mature bone cells and osteoclasts break down and reabsorb bone (Figure 6) [5-6].

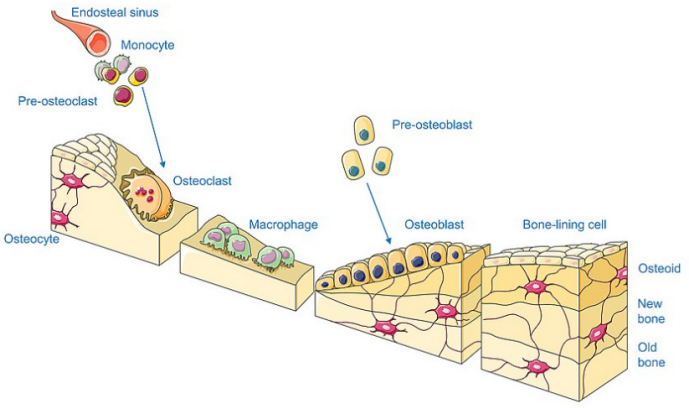


Figure 6: Our schematic representation of the bone remodeling process.

Peak bone mass

The bone mass refers to the amount of bone present, both organic and mineral. The bone mass increases during adolescence and reaches peaks at the end of adolescence at about twenty years. The maximum amount of bone acquired at the time of bone maturity is known as peak bone mass Figure 8.

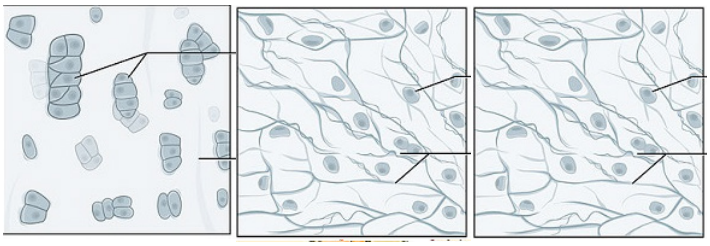
Cartilage

The cartilage is not directly affected by osteoporosis; we mention it because it is the first stage of embryogenic development of bones and covers the articular surfaces of bone segments where it forms a translucent layer, which has the function of facilitating the sliding between the articular heads.

Composition of the cartilage

- *Basic substance: Glycosaminoglycans and proteoglycans, not calcified*
- *Cells: Chondrocytes, chondrosarcobacteria (Secretion matrix and fibres)*
- *Fibre: collagen, elastin*

Types of cartilage: Hyaline, Elastic, Fibrous (Figure 7).



A B C

Figure 7: Our drawing of different cartilages: Elastic C, Fibrous B, And Hyaline A.

Loss of bone mineral and mass

Osteomalacia

Osteomalacia, is a failure to mineralize bone.

Usually, osteomalacia results from vitamin D deficiency (serum 25-hydroxyvitamin D concentrations ≤30 nmol/L) and inability to absorb dietary calcium and phosphorous across the small intestine.

Blood calcium and phosphorus concentrations are tightly controlled by parathyroid hormone (PTH). Increased PTH stimulates the activity of bone remodeling - both resorption and formation, which are always coupled. We mentioned the cells responsible for bone remodeling Osteoblasts, Osteoclasts, and Osteocytes.

The osteoclast releases calcium and phosphorus from the bones to restore calcium concentrations in the blood, and the osteoblast mobilizes to replace the reabsorbed bone. During osteomalacia, however, calcium and phosphorus deficiency causes an incomplete mineralization of the newly secreted bone matrix. In severe cases, the newly formed, mineralized bone loses its rigidity and can deform under the stress of body weight.

Osteopenia

Briefly, osteopenia and osteoporosis are different degrees of reduced bone mass. While osteomalacia is characterized by low mineral content and high matrix content, osteopenia and osteoporosis result from low levels of both. As defined by the World Health Organization (WHO), osteopenia precedes osteoporosis and occurs when its BMD is between 1 and 2.5 standard deviations (SD) below that of the average young adult (30 years of age) [5].

Osteoporosis

Osteopathy characterized by reduction of bone mass and deterioration of the structure resulting in increased fragility and high risk of fractures. The ratio of mineral to organic is normal, unlike osteomalacia where the defect is borne by the mineral component [5]. Osteoporosis is a condition of increased bone fragility and susceptibility to fracture due to loss of bone mass. Clinically, osteoporosis is defined by the World Health Organization (WHO) as a BMD (Bone Mineral Density) that is greater than 2.5 standard deviations (SD) below the mean of a young adult; the value is expressed with T- score. It has been estimated that fracture risk in adults is approximately doubled for each SD reduction in BDM. Common sites of osteoporotic fracture are the hip, femoral neck, and vertebrae of spinal column — skeletal sites rich in trabecular bone (Figure 8) [7-9].

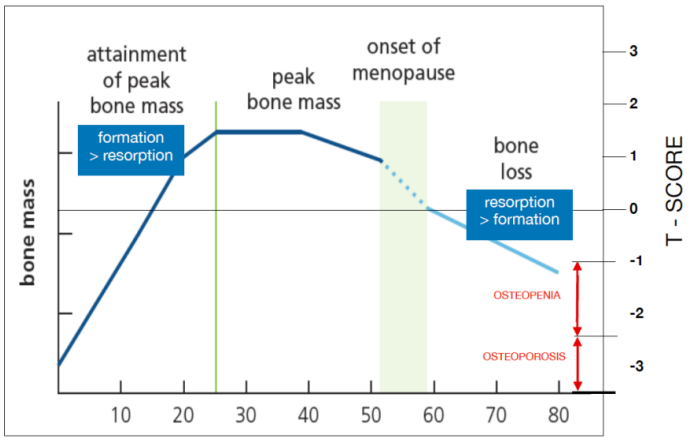


Figure 8: Evolution of Bone mass during aging (Modified by International Osteoporosis Foundation 2013).

The T-score: It is calculated by subtracting the bone mass value (BMD) of the patient from the reference value of normal subjects of about 30 years (YN), age at which the bone mass is at maximum and the risk of fractures at minimum. The obtained value is divided by the standard deviation (SD).

T-score= (BMD-YN)/SD

Pathophysiology

Biological causes of Osteoporosis

In adults, the daily removal of bone mineral, resorption, is balanced by an equal deposition of new mineral for maintain bone strength. When this balance tips toward excessive resorption, bones weaken and over time can become brittle and prone to fracture over time (osteoporosis). This continual resorption and re-deposition of bone mineral, or bone remodeling, is intimately tied to the pathophysiology of osteoporosis. Understanding how bone remodeling is regulated is the key to the effective prevention and treatment of osteoporosis [6].

Skeleton is alive and must be able to grow, heal, and respond to its environment, in this remodeling play UN crucial role. However, during ageing, daily-remodeling leads to a gradual resorption of the minerals in the cortical layer and in the bone cavity itself leads to an inexorable loss of trabecular bone and a widening of the bone cavity. The thinner cortical layer is, the more susceptible it will be to resorption later in life. Hormones are possibly the most crucial modulators of bone formation. It is well established that oestrogen, parathyroid hormone and to a lesser extent testosterone directly or indirectly via the conversion into oestrogen are essential for optimal bone development and maintenance. Among these, oestrogen is now believed to have the most direct effect on bone cells, interacting with specific proteins, or receptors, on the surface of osteoblasts and osteoclasts. Bone resorption is particularly evident in women immediately after menopause but osteoporosis is most likely to develop when the peak in bone mass, have reached within the first 20-25 years of life, is not optimal (Figure 8).

The bone mass can be evaluated with non-invasive methods (bone densitometry, etc.) applicable both in the prevention phase and to monitor the effect of a possible therapy. In addition, there is a range of biochemical assays on plasma and urine that can provide information on the speed of bone turnover [5].

Osteoporosis has a peak incidence in mature age and can be primary, metabolic type or secondary if it depends on different causes
Primary osteoporosis is itself classified into 2 types:

- Type 1 - postmenopausal osteoporosis
- Type 2 - Senile osteoporosis

Secondary osteoporosis reflects the incidence of disease and/or clinical conditions and/or chronic use of drugs with which it is associated.

Diagnosi Osteoporosi

There are two types of diagnostic methods for osteoporosis: Bioumoral and Instrumental.
A) Biohumoral diagnosis: By Specific biomarkers [10]

Marker of neoformation

Bone isoenzyme of alkaline phosphatase, osteocalcin, procollagene propeptides type I)

Markers of bone resorption

(pyridinoline, desoxypyridinoline, telopeptides N or C type I collagen terminals).

B) Instrumental diagnosis: Bone densitometry, spinal MRI

Treatment of Osteoporosis

We distinguish two types of treatment, Pharmacological and Non Pharmacological.

I) ***Pharmacological treatment***

For this treatment are used several medications: Bifosfonati, Denosumab, Nonhormonal Therapy, Hormone Replacement Therapy, Parathormone, Strontium Ranelato, Selective Estrogenic Receptor Modulators (SERM) [11-12]. Most of these drugs have shown results of dubious efficacy, compared to significant side effects even severe.

II) ***Non pharmacological treatment*** of osteoporosis includes food supplements and physical activity.

Essential nutrients for the skeletal system

Optimal qualitative and quantitative intake of certain nutrients is essential for the proper functioning of the skeletal system and for the correct osteogenesis. Among the most important are the Macroelements: Calcium, Magnesium, and Microelements: Zinc, Vitamin D, Vitamin K, Boron [13-17]. Silicon deserves a special mention: silicon plays an important role in promoting the deposition of calcium in immature bone tissue and its contribution accelerates the mineralization of bones. In addition, this element stimulates collagen production and the maturation of osteoblasts Table 1.

Nutrient	Recommended Dietary Allowance	Median Intake
Vitamin D	600-800 IU	150-300 IU
Calcium	1000-1200 mg	735 mg
Magnesium	320-420 mg	243 mg
Silicon	*40 mg for bone health	21 mg
Vitamin K	90-120 µgm	70-80 µgm
Boron	*3 mg for bone health	1 mg
Vitamin C	75-90 mg	103 mg
Copper	0.9 mg	1.1 mg
Zinc	8-11 mg	9.6 mg
Manganese	1.8-2.3 mg	2.8 mg

Table 1: Common Nutrients for Bone Health.

Food supplements

Among the supplements most used in osteoarticular diseases, we must mention the following [18-20].

Glucosamine - In osteoarthritis, an additional supply of glucosamine provides chondrocytes with enough raw material to compensate for the imbalance between degradation and renewal of cartilage, allowing a faster restoration.

Chondroitin sulfate - Increases the concentration of glycosaminoglycans in cartilage and limits its excessive degradation. In fact, its function is to form bonds with collagen fibrils. An effect has been demonstrated Inhibitory of this substance against lithic enzymes, such as collagenase and elastase.

Type II Collagen - Oral administration of this protein has brought improvements to Osteoarthritis, based on the mechanism of down regulation of autoimmune diseases.

Jaluronic Acid - Acts as a lubricant within the synovial fluid.

MSM (methylsulfonylmethane) - Natural source of sulfur, is a natural analgesic. It has anti-inflammatory activity due to the stimulation of cortisol synthesis (hormone that improves the permeability of cell membranes). It can also be considered a good antioxidant *factor* [13-15]. The supplements based on are vitamins and minerals are used too. The most widely used vitamins are Vitamin D3, Vitamin K, Vitamin C, Vitamin E and Vitamins B (especially B6 and B12) [16-19].

Insted among the minerals a general and widespread contribution of Calcium, Magnesium, Zinc, Boron, Silicon, Selenium, Manganese.

The role of silicon

It has long been known for a long that organic silicon plays a fundamental role in osteogenesis as it stimulates the synthesis of collagen and the formation of osteoblasts. It has also been described an anti-inflammatory and painkiller activity related to the use of this element Figure 9.

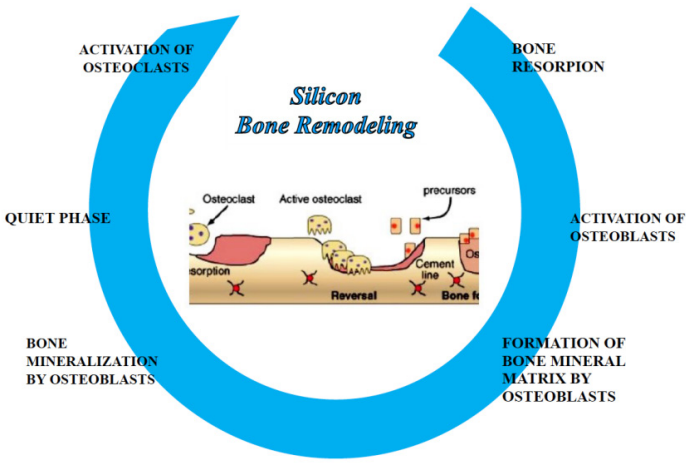


Figure 9: Silicon activates the prolyl-hydroxylase enzyme, present in the granular endoplasmic reticulum of the osteoblast cytoplasm. The enzyme governs the formation and bone mineralization.

Modified by: Alberghini Maltoni Andrea; The determining role of silicon in bone formation - review and clinical results, Jour. Clin. Med. And Therap. 2018, Vol.3 No. 1:05.

In vitro studies and in vivo studies have also added to the evidence that Si may be beneficial for bone formation and for bone and connective tissue health. Silicon is known to enhance proliferation, accelerate differentiation, promote matrix synthesis, and enhance bone formation [20-24].

Essential for bone formation is the synthesis and deposition of collagen type I, which constitutes 90% of the total organic extracellular matrix in mature bone, by preosteoblasts or early-undifferentiated osteoblast-like cells. In this synthesis, metabolic role and a structural role have been attributed to Si. Recent research have revealed the physiological role of Si in bone and connective tissue formation by observing the high concentrations of Si and apical accumulation of Si at the growing front of bone mineralization, and matrix polysaccharides and proteins synthesis with Si supplementation.

Furthermore, Si in the form of orthosilicic acid has been shown to induce type I collagen secretion and gene expression by osteoblasts and osteoblast-like cells for bone cell maturation and bone formation. Besides involvement in bone health, Si by effecting connective tissue formation has been shown to affect the skin too. These cell based observations have also been verified by two cross-sectional epidemiological studies and associated Si intake with higher bone mineral density (BMD), increase in trabecular bone volume, and less hip bone fractures Figure 8. Illustrates the involvement of Si in bone strengthening. However, silicon has limited using due to its poor intestinal absorption. In the forms of salt found in nature (natural mineral forms such as vegetable-silicates) this trace element, is difficult to assimilate at the biological level. Inorganic silicon is not absorbed, in order to perform its function as a bone restorer it must be taken in organic form.

Organic silicon G5

Organic silicon G5 is a new biological source for bone protection and the prevention and treatment of osteoporosis and arthropathies. Recently an organic form of silicon has been patented, Silicon G5, which has shown good intestinal absorption and allowed its use as a dietary supplement [25-28].

The unique characteristics of Organic Silicon G5, can be summarized as follows: [29]

- Organic silicon G5 is the most bioavailable form of silicon;
- The absorption of organic silicon G5®, is considerably higher than the other known silicon supplements, at least four times higher than the other known forms of integration; Figure 10.
- Organic silicon G5® is not only very easily absorbed by the organism, but is also metabolized as biological silicon ("orthosilicic acid");
- Silica in its bioactive forms, plays an important role in collagen synthesis;
- Silicon activates the prolyl-hydroxylase enzyme, present in the granular endoplasmic reticulum of the osteoblast cytoplasm. The enzyme governs the formation and bone mineralization.

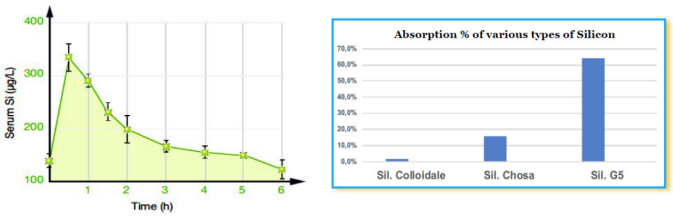


Figure 10: Absorption of Organic Silicon G5 and comparison with other types of Silicon (Modified from SILICIUM ORGANIQUE LLG5-2014).

Formulation of the food supplement based on organic silicon

Starting from these properties of Organic Silicon G5, in the prevention and treatment of osteoporosis and osteoarticular diseases, in a previous work, to which reference is made [29], we have tested a combination formulation of Silicon G5 with other nutrients on a restricted case study. The composition adopted was as follows:

Organic silicon G5, Magnesium, Zinc, Vitamin D3, Vitamin K2, Bromelain, in these quantities: Organic silicon G5: 300 mg, Magnesium: 400 mg, Zinc 35 mg, Vitamin D3: 1000 U.I. Vitamin K2: 35 mcg and gastro-protected Bromelain: 100 mg (2,500 GDU/g).

*The supplement was produced as a galenic preparation, by an accredited pharmacy. The supplement has been designed to obtain a specific and synergistic activity on Collagen, since Collagen is considered the common denominator target pathogenetic osteoarticular diseases a*dministered in sachets as a soluble powder.

Examination of the properties of the individual components

The formulation has been designed to obtain a specific and synergistic activity on Collagen since Collagen is considered the common pathogenic denominator of osteoarticular diseases. The supplement was produced as a galenic preparation, by an accredited pharmacy.

The supplement has been designed to obtain a specific and synergistic activity on Collagen, since Collagen is considered the common denominator target pathogenetic osteoarticular diseases.

Examination of individual components:

Organic Silicon G5:

Organic silicon G5, as seen above, plays a central role in the structural organization of glycosaminoglycans and polyuronides. In addition to the effects already described for Silicon G5 on the synthesis of collagen, we must mention the specific mechanism of Molecular Action on connective.

It's been provened that silicon can function as a biological cross-linking agent and contribute to the architecture and resilience of connective tissue. As for the single polysaccharide molecules, Silicon G5 could work in several ways:

(a) It could connect different portions of the same polymeric saccharide chain, establishing a secondary structure and controlling molecular shape.

(b) It could link different polysaccharide chains to each other.
Si may contribute to the very high molecular size of glycosaminoglycans and polyuronides in their natural state.

(c) Si could also link acid mucopolysaccharides to proteins. Almost all glycosaminoglycans, and many other polysaccharides, occur in nature primarily as protein-polysaccharide compounds [30].

Si could establish a bridge between glycosaminoglycans and collagen, or the globular protein found in the ground substance of connective tissue [31]. Such a link could exist aside from the well-documented polysaccharidexylosyl-serine-protein bridge and similar links found in proteoglycan molecules. Combined therapy of ch-OSA and Ca/Vit D3 had a potential beneficial effect on bone collagen compared to Ca/Vit D3 alone which suggests that this treatment is of potential use in osteoporosis [32].

Magnesium

Several direct and indirect mechanisms contribute to the effects of low magnesium on bone density:
Low magnesium can directly affect the bone by altering the structure of apatite crystals; magnesium deficiency is also associated with reduction of PTH and 1,25(OH2) D levels and low-grade inflammation and endothelial dysfunction, with a well-known relation between inflammation and bone loss [16,33].

Vitamin K2

Vitamin K2 functions in the post-translational modification of a number of vitamin K-dependent proteins such as osteocalcin, a bone protein containing gamma-carboxyglutamic acid, discovered in 1975 [34].

Gamma-carboxylation of the glutamic acid in osteocalcin is vitamin K2 dependent and involves the conversion of glutamic acid residues (Glu) to gamma-carboxyglutamic acid residues (Gla). A number of calcium binding proteins, such as calbindin and osteocalcin, contain gamma-carboxyglutamate. These proteins are involved with calcium uptake and bone mineralization [35-37].

Osteocalcin is synthesized in osteoblasts. Because steocalcin that is not carboxylated cannot bind to hydroxyapatite, serum levels of osteocalcin are a good biochemical marker of the metabolic turnover of bone.

Vitamin D3

The main role attributed to vitamin D is that of regulatory factor of bone metabolism and homeostasis of calcium and phosphorus in relation to parathyroid hormone (PTH). Serum vitamin D concentrations are inversely proportional to PTH (with which negative feedback exists); low levels of vitamin D cause bone tissue resorption while optimal levels facilitate the absorption of calcium and phosphorus from the kidney and intestine. The effects of vitamin D are extrinsic at the intestinal, bone, renal and parathyroid levels [38].

At the bone level 1,25(OH)2D3 causes an increase in bone resorption, an action that occurs in synergy with PTH. Mature osteoclasts have neither PTH nor 1.25(OH)2D3 receptors, so it is believed that the two hormones increase bone resorption by stimulating the maturation of osteoclasts and/or interacting with osteoblasts and medullary stromal cells. Such interaction would result in the release of cytokines capable of stimulating the activity of mature osteoclasts [39]. Finally, vitamin D in addition to promoting an adequate supply of calcium and phosphorus necessary for bone mineralization has an important role in regulating osteoblastic.

The main metabolite of vitamin D responsible for calcium mobilization is 1α25(OH)2D3, which is 80 times more powerful than 1αOHD3 and stimulates bone resorption by stimulating RANKL expression in osteoblasts. Effects caused by the administration of 1α(OH)2D3 and 1α(OH)D3 are due to the suppression of bone resorption, although the mechanism is still unknown.

Zinc

A recent study showed that the mean dietary intake of magnesium, zinc and calcium in post-menopausal women with low bone density were significantly lower than recommended dietary allowance. Zinc plays a pivotal role in the regulation of bone homeostasis [16]. Many zinc-related proteins are found to involve in the regulation of cellular function in osteoblasts and osteoclasts. Zinc stimulates cell differentiation, cell proliferation, and mineralization in osteoblasts through gene expression of various proteins including type I collagen, alkaline phosphatase, and osteocalcin. Furthermore, zinc inhibits osteoclastic bone resorption suppressing osteoclast-like cell formation, inhibits action of RANKL in pre-osteoclasts and stimulates gene expression of OPG in osteoblastic cells [40].

Starting from this experience, positively tested, we have decided to extend the case studies to a wider number of patients on which to confirm the effectiveness and safety of the supplement.

For this case study, we used a supplement of identical formulation, but registered and certified by the Italian Ministry of Health, with the brand Silicos. The product comes in soluble powder, gluten free, in a pack of 30 sachets. The rationale of the formulation is given in the following diagram in the form of a diagram showing the synergistic activity of the individual components on bone remodeling Figure 11.

Study Design and Methods

Also in this study, we have used the same design and method of investigation and the same evaluation criteria of the previous work [29].

Simple open-label works with control of hematological and instrumental parameters (Data on reserved files).

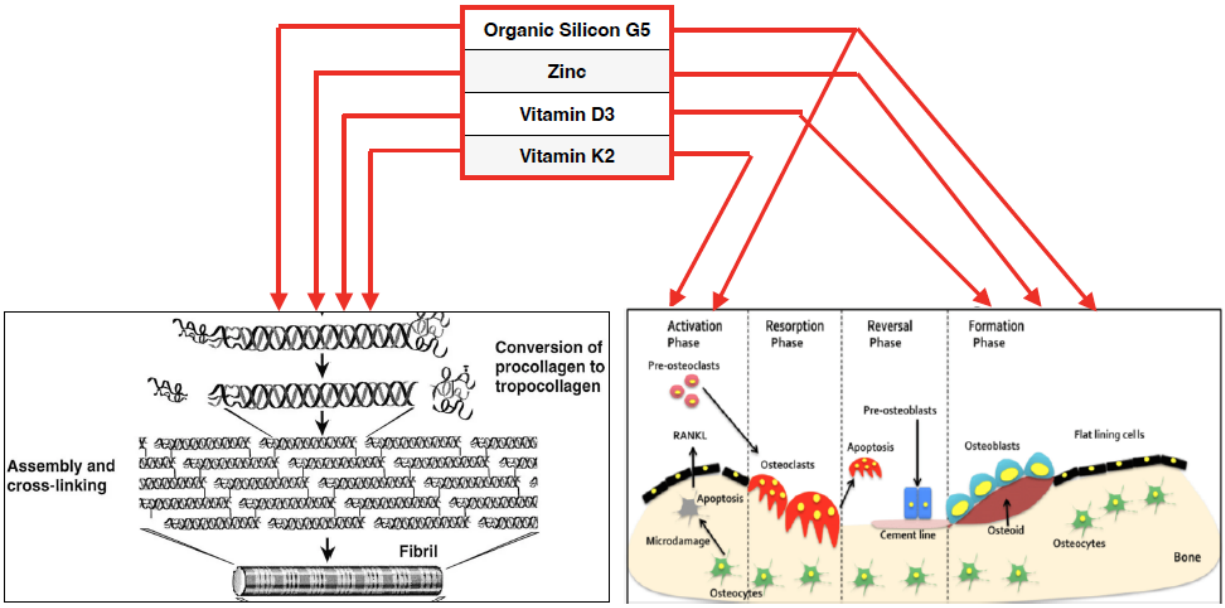


Figure 11: Synergistic activity of microelements on collagen formation and bone remodeling.

T-SCORE Time 0	T-SCORE Six Months After	328 WOMEN		T-SCORE Time 0	T-SCORE Six months after	322 MEN
-2,20	-2,00	45	BDM SPINE	-1,98	-1,64	21
-2,35	-2,11	48		-2,00	-1,87	43
-2,63	-2,15	56		-2,09	-1,29	56
-2,74	-2,20	67		-2,11	-1,43	65
-2,14	-1,98	36		-2,14	-1,98	46
-2,51	-2,03	29		-2,31	-2,00	38
-2,81	-2,15	33		-2,18	-1,89	35
-1,97	-1,74	14		-1,99	-1,57	18
-2,38	-2,01	47	BDM FEMUR	-2,38	-2,01	47
-2,41	-2,05	39		-2,41	-2,00	36
-2,77	-2,00	59		-2,77	-2,03	59
-2,33	-2,07	41		-2,33	-1,99	44
-2,21	-1,96	37		-2,21	-1,96	31
-2,55	-2,11	46		-2,55	-2,02	46
-2,62	-2,16	43		-2,62	-2,10	43
-2,19	-1,89	16		-2,19	-1,89	16

Table 3: Our Bone Mineral Density T-Score Results.

Questionnaire and Registration

Administration of a questionnaire for an anamnestic survey. The first part of the questionnaire relates to personal history, with regard to predisposing diseases.

Other Collected Data: Age, ethnicity, smoking, physical activity, BMI, food (Some of these data are not reported).

Criteria for Inclusion

Patients 60 years or more of age; of both sexes who have been asked for informed written consent; Patients enrolled with various degrees of Osteopenia and Osteoporosis diseases were checked with routine examinations at the beginning and end of treatment by physicians.

Criteria for Exclusion

Patients were excluded according to the following criteria: Patient with infectious diseases of any nature, subject to blood transfusions, with renal failure as defined by serum creatinine > 200μmol/L, abnormal serum ferritin level (normal range: 11–250μg/L), concomitant medication treatments like Corticosteroids, Anti-inflammatory and antiosteoporous. Those treated with anti-inflammatory drugs were subjected to a two-month washout period before starting treatment.

BIOMAKERS EVALUATION OF PATIENTS FROM BASELINE (TIME 0) TO FINAL TIME (AFTER 6 MONTHS)				
NUMBER OF PATIENTS	328 WOMEN		322 MEN	
AGE (YEARS)	60,0 ± 5,6			
BONEMARKERS	**Initial Time -0**	**Final Time - After 6 Months**	**Initial Time -0**	**Final Time - After 6 Months**
OC (ng/mi)	14,89 ± 2,31	16,21 ± 2,00	16,01 ± 2,43	17,03 ± 2,00
BAP (µg/l)	4,31 ± 5,43	5,56 ± 4,63	7,83 ± 6,01	8,32 ± 4,01
DPI (µmol /Cr)	5,75 ± 2,34	4,11 ± 1,34	5,87 ± 1,63	3,98 ± 0,83
BASELINE CHARACTERISTICS OF PATIENTS (N = 650) MEAN ± SD, A : p < 0,05				

Table 4: BOMERKERS: Osteocalcin (OC), Bone specific Alkaline Phosphatase (BAP), deoxypyridoline (DPD) AVERAGE VALUES.

Subjects

From April 2020 to October 2021, 19 months, 650 patients were selected and evaluated, among the more than 7,000 who used the same product Silicos. The patients were divided into two groups: a group that collected osteoporotic patients or osteopenic patients formed by 328 women, and a group of 322 men.

Measurements

Both groups were subjected to basic clinical examination at each visit including measurement of IBM, blood pressure and heart rate. Blood samples and single void urine samples were collected from fasting subjects at baseline and after 6 months supplementation to evaluate the safety parameters before and after the treatment.

The results of the other routine blood tests, which are not relevant for assessing treatment effectiveness, are not reported in this work. We have reported only the instrumental BMD results and the mean haematochemistry values relevant to the markers of bone remodeling. We adopted the average values of the observations because it would have been impossible to report the results of all the values of the individual patients Such a case study, even with the methodological limits adopted, assumes in any case a significant value , for the evaluation of the effectiveness and tolerability of the formulation.

Osteoporotis patients

650 Patients were treated for six months at the dosage of one sachet a day of Silicos.

Results relating to instrumental and emochemical exams Table 3.

BMD

Most of the evidence for the effectiveness of preventive treatment comes from patients who had already suffered a previous fracture of slight magnitude detectable only radiographically, indicative of structural bone impairment and prognostic of possible further major fracture events. In fact, this condition represents a definitive indication to a preventive treatment, even in the case of a normal BMD.

Except for selected cases, densitometry does not add anything to our clinical evaluation in the decision to start a treatment in the monitoring of the treatment itself. We believe that higher prognostic value assume the variations of bone markers over time as indicators of physiological bone remodeling Table 4.

Discussion and Conclusion

Osteoporosis is a metabolic disease with multifactorial etiology, which has an increasing incidence with the ageing population, with particular penetration in the female sex. It is a devious pathology because it does not have any obvious symptoms until the event of bone fractures, which involve hospitalization and a significant social cost. The best strategy for reducing fracture events is the prevention that should be adopted from the onset of menopause in women and andropause in men. Prevention is carried out with screening of blood chemistry markers of bone metabolism and with specific instrumental examinations such as bone densitometry and Nuclear Magnetic Resonance Imaging.

Double-energy x-ray absorbency (DEXA) is considered the preferred technique for densitometric evaluation and is considered a non-invasive, reproducible, predictive tool for short and long-term fracture risk, Capable of measuring bone very fairly precisely and accurately and of estimating the risk of osteoporotic fractures accordingly. However, this evaluation is certainly not conclusive and very reliable, in the absence of other evaluations of Bone markers more relevant and metabolically sensitive to bone homeostasis, especially if evaluated in their temporal progression.

DEXA allows BMD to be measured at all skeletal sites, but those most frequently measured are the lumbar spine, the proximal femur, the proximal and distal radium. The test expresses the bone density in absolute terms in grams of ore per square centimetre and compares the value found with a normal adult population (value known as T-score) or the expected value by age and sex (Z-score).

The threshold for diagnosing the presence of osteoporosis indicated by the World Health Organization corresponds to a T-score of less than -2,5 obtained with DEXA technique.

This test has a predictive value compared to vertebral fractures in post-menopausal women and is considered useful in evaluating the BMD's ongoing follow-up.

In our study, we have adopted both methods of investigation for the follow-up of our case studies. The results show that all the parameters and indices of bone metabolism evolve positively, even within the limits of case studies and experimental design, and are suggestive of a good effectiveness. In conclusion, we can say that the formulation of our supplement is a valid alternative to pharmaceutical therapies, not always effective, with the undoubted advantage of total absence of adverse phenomena.

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