

# Study of a Standardized Plant Extract Used as an Anti-Inflammatory Drug to Reduce Joint Pain

MARIA TOTAN<sup>1,3</sup>, ELISABETA ANTONESCU<sup>1,2\*</sup>, LAVINIA DUICA<sup>1,4</sup>,  
CORINA ROMAN-FILIP<sup>1,2</sup>, SINZIANA CALINA SILISTEANU<sup>5</sup>

<sup>1</sup> Lucian Blaga University of Sibiu, Faculty of Medicine, 2A Lucian Blaga Str., 550169, Sibiu, Romania

<sup>2</sup> City Clin Emergency Hosp, 2-4 Corneliu Coposu Str, Sibiu 550245, Romania

<sup>3</sup> Clin Pediat Hosp, Clin Lab, 2-4 Pompeiu Onofreiu Str, Sibiu 550166, Romania

<sup>4</sup> Psychiat Hosp Doctor Gheorghe Preda Sibiu, 12 Doctor Dumitru Bagdazar Str, Sibiu, Romania

<sup>5</sup> Stefan cel Mare University of Suceava, Department of Health and Human Development, 13 Universitatii Str., Suceava, Romania

**Abstract.** *This study was to demonstrate the role of a natural anti-inflammatory, in reducing pain, inflammatory process and increasing joint mobility in elderly patients diagnosed with knee osteoarthritis. Osteoarthritis off knee affect the articular cartilage, but also the articular capsule, leading to disability. This natural anti-inflammatory has a complex composition: extract de Boswellia serrata 300 mg, extract de curcuma 100 mg, extract Pinus pinaster 80 mg și extract de Zingiber officinale 40 mg. The combination of herbal products, which have no side effects, with electrotherapy and kinetotherapy can be a real success in this category of patients, also influencing their well-being.*

**Keywords:** *knee, osteoarthritis, natural anti-inflammatory*

## 1.Introduction

Osteoarthritis is a part of the chronic degenerative disorders, which affect the articular cartilage, but also the articular capsule, leading to disability. One of the most affected joints is the one of the knee with implications on gait, stability and balance [1].

The elderly people have over 80% radiological changes in the knee, with alteration of the subchondral bone structure, articular cartilage impairment and the appearance of osteophytes by marginal bone hypertrophy [2] with alteration of the subchondral bone structure, articular cartilage impairment and the appearance of osteophytes through the hypertrophy marginal bone [3, 4]. In the elderly people, osteoarthritis is considered a public health problem [5], which involves high costs and affecting the patients' quality of life.

Besides pain, it presents the limitation of range of motion, walk instability, postural and gait impairment [6,7]. Research has shown the involvement of cytokines, especially of the interleukin -1 and 17, as well as tumor necrosis factor TNF  $\alpha$  in stimulating the degradation of some protein, resulting in accelerated cartilage destruction. Doing physical exercises, due to the synthesis of neurotrophins and the improvement of the neuroplasticity has a role in the psychic recovery of the cognition of the patients with osteoarthritis [8].

The recovery of patients diagnosed with osteoarthritis involves a multidisciplinary team, especially in the elderly people with comorbidities [9].

The treatment of osteoarthritis (analgesic , anti-inflammatory, decontracting, fibrinolytic purposes) involves the application of physiotherapy , application of low and medium frequencies [10,11] and ultrasound [12,13] techniques aiming at reducing the pain and inflammatory process in the short term and in the medium and long term, by preventing and fighting joint pain, regeneration defects and functional deficiencies that can cause disability [14].

The pathogenesis of the knee osteoarthritis involves several factors, among them a joint load [15], the modification of the biomechanical elements at the level of body segments, or changes of the hormonal system and cytokine production [16,17].

\*email: [elisabeta.antonescu@ulbsibiu.ro](mailto:elisabeta.antonescu@ulbsibiu.ro)

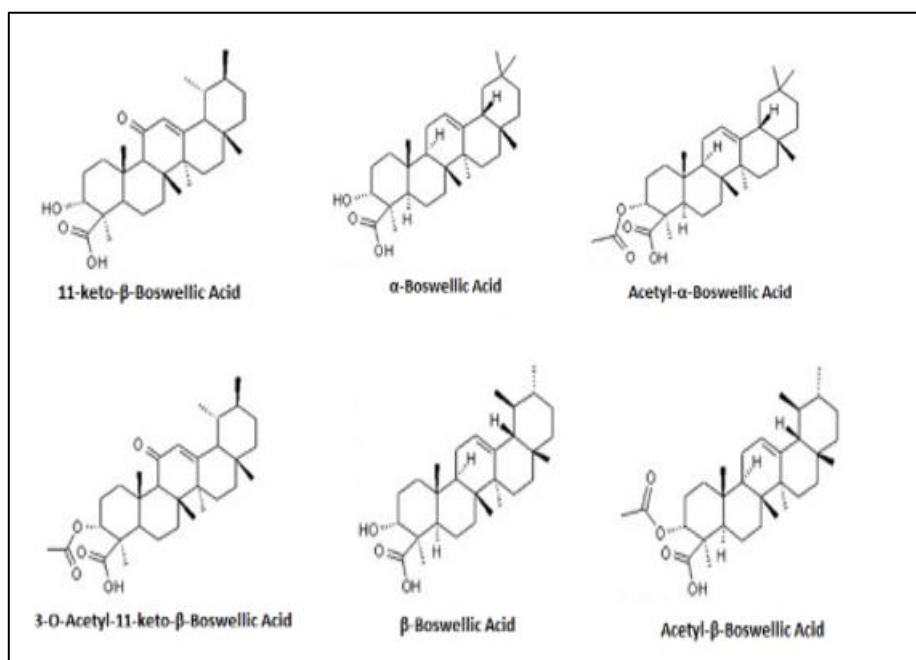
An important role in ensuring the functional status of the knee is represented by the kinetic techniques within the kinetotherapy with the role of prophylaxis of the muscular atrophy for quadriceps, restoring the joint mobility, ensuring the correct static posture and ensuring the elements for a normal gait. [18],[19]. In his studies (2015) Cochrane [20] identified the importance of physical exercise in improving pain and functional status in patients diagnosed with knee osteoarthritis. , hypothesis confirmed by Fransen et al. (21)

The guidelines recommend the practice of the physical exercise to patients with knee osteoarthritis (even if the results are beneficial in the short term, up to 6 months) [1] and the use of non-steroidal anti-inflammatory drugs used locally and not orally due to reactions that may occur at the digestive tract level, cardiovascular and renal [22,23,24,25]. The recommendations of ACR/EULAR (The American College of Rheumatology/ The European League Against Rheumatism) indicate the combination of pharmacological and non-pharmacological treatment to ensure optimal results in the treatment of the knee [26,27,28]. Natural treatments are also used for other pains[29]. Lately the treatment of osteoarthritis mentions the use of herbal treatments as well, especially in elderly patients [30].

There are natural anti-inflammatory drugs that contain standardized extracts that generate a synergistic effect. To produce a standardized plant extract, a certain technological process follows by which one or more chemical components with therapeutic effect are concentrated and some unnecessary components are removed. The production method, controlled and validated [31], results in a "standardized" product that ensures a well-defined therapeutic potency.

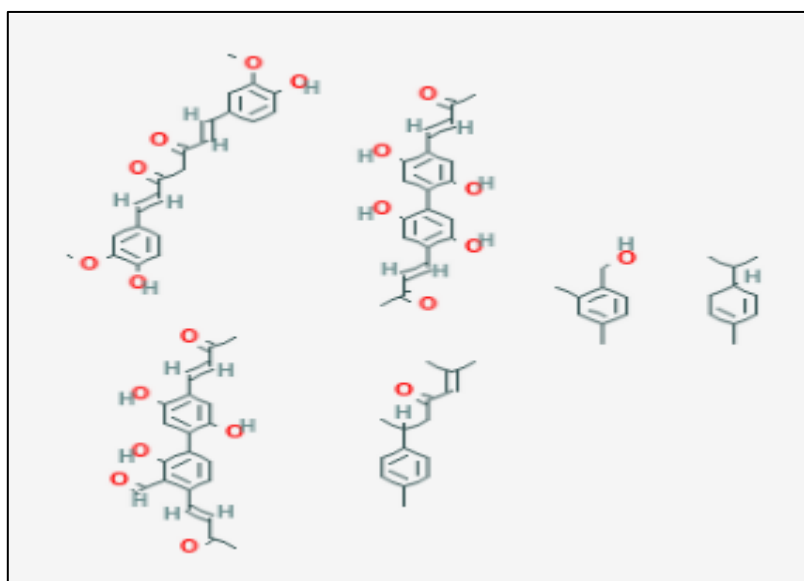
An example is a natural anti-inflammatory with a complex composition: *Boswellia serrata* extract 300 mg, Turmeric extract 100 mg, *Pinus pinaster* extract 80 mg and *Zingiber officinale* 40 mg extract. All these components act synergistically and give the product anti-inflammatory, analgesic, antioxidant properties. It is administered by 2 capsules/day. This product has no side effects, it can be used for a long period.

The boswellic acids (Figure 1) are known to be specific inhibitors in the synthesis of leucotrienes from arachidonic acid (in vitro). *Boswellia* has similar action to non-steroidal anti-inflammatory drugs, but without side effects.



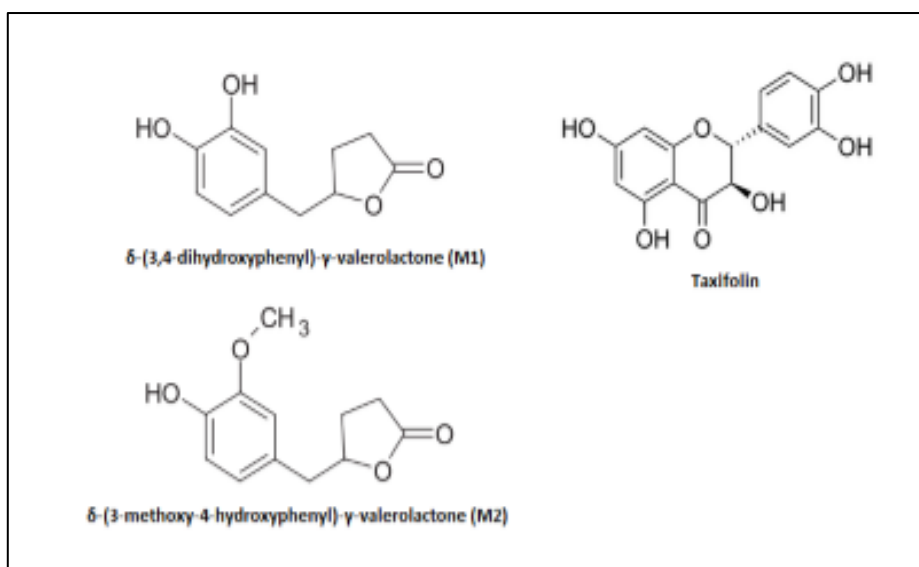
**Figure 1.** Chemical formula for Boswellic acids

The boswellic acids block leukotriene synthesis (they play a role in inflammation) and contribute to the diminishing of the inflammatory reaction and to the decreasing of the joint cartilage impairment, by preventing the production of cartilage-destroying enzymes, and at the same time by reducing urinary elimination of hydroxyproline, hexosamine and of uronic acid, favoring the cartilage restoration process. The consequences of this action are the reduction of the pain and of the periarticular edema, but also the improvement of the blood circulation in the inflamed tissue. Boswellia has fortifying action on cartilage and bone tissue structures. The turmeric has an anti-inflammatory effect, it limits the action of lipooxygenase and cyclooxygenase. The research shows that the curcumin molecule (Figure 2) models the inflammatory response by regulating cyclooxygenase 2 activity, lipooxygenase and inhibiting cytokine production, the tumor necrosis factor  $\alpha$  of interleukins IL-1, IL-2, IL-6, IL-8, IL-12.



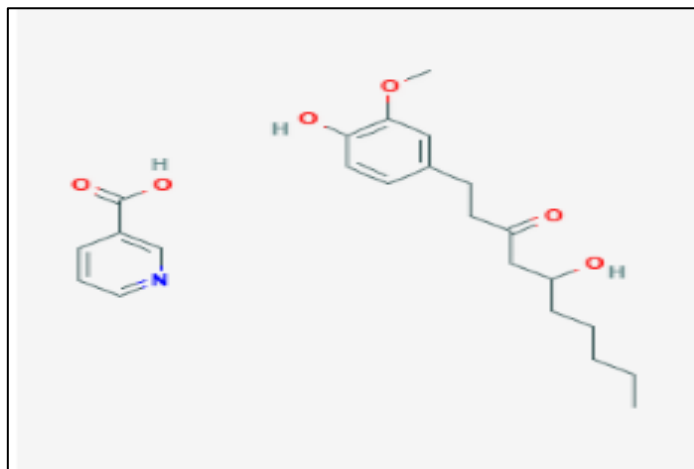
**Figure 2.** Chemical formula for Curcuma Longa

Pycnogenol is a proanthocyanidin, meaning a complex of bioflavonoids extracted from the bark of the Pinus maritime tree (Figure 3). It absorbs rapidly into the body (20 min) and has an action of up to 72 h, having a protective role against free radicals.



**Figure 3.** Chemical formula for Pycnogenol

*Zingiber Officinallis* (Figure 4) contains the following active pharmacological ingredients: ginger and zingeron, which have anti-inflammatory action (by suppressing prostaglandin synthesis and inhibiting cyclooxygenase, reducing leukotriene biosynthesis, reducing inflammation and pain), analgesic, antioxidant.



**Figure 4.** Chemical formula for *Zingiber Officinallis*

## 2. Materials and methods

The objective of the study was to demonstrate the role of a natural anti-inflammatory with a complex composition, in reducing pain, inflammatory process and increasing joint range of motion in elderly patients diagnosed with knee osteoarthritis.

We consider that the combination of herbal products, which have no side effects, with electrotherapy and kinetotherapy can be a real success in this category of patients, influencing their well-being.

The objectives pursued in this trial were: reduction of pain, increase of static and dynamic stability, increase of joint range of motion, correction of gait, increase of the quality of life of this category of patients

This observational study was conducted in an outpatient setting for a period of 6 months, complied with the rules of ethics and medical deontology in force and involved a number of 64 patients who were informed about the study and gave their consent.

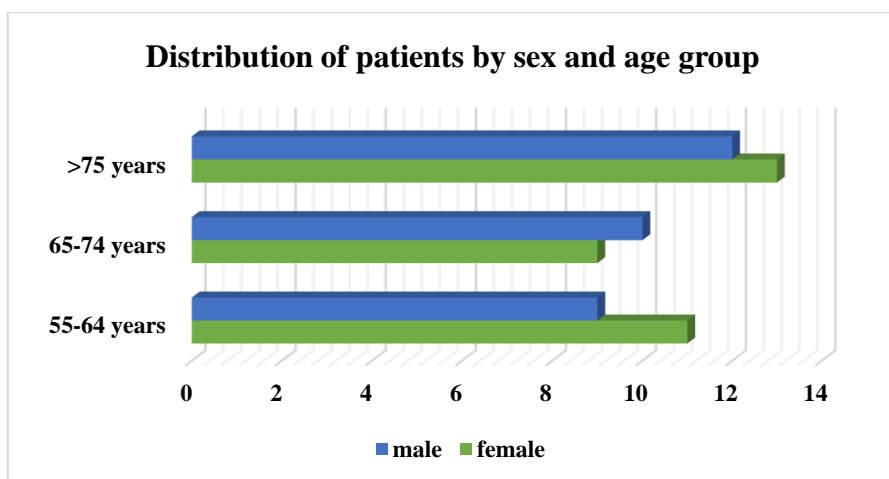
The criteria for inclusion in the study were: the age over 55 years, the diagnosis of primitive osteoarthritis of the bilateral knee, the evolution of the disease of at least 5 years, the compliance in the application of treatment and compliance with the indications given until returning to control, not having received physical treatment in the last 6 months and the consent to participate in the study.

The exclusion criteria from the trial were: secondary osteoarthritis to traumatic knee disorders (fractures, dislocations, sprains), association with chronic rheumatic diseases (ankylosing spondylitis, rheumatoid arthritis, gout) or neurological disorders with manifestations in the lower limbs, cardiovascular and decompensated lung diseases, under the age of 55, persons who did not give their consent to participate in the trial.

The treatment was complex and included: hygienic-dietary regimen (adequate diet, movement, static and dynamic posture), pharmacological (herbal medicine administration) and specific techniques of electrotherapy and kinetotherapy. The patients were informed about these elements of the recovery program and received all indications on the daily caloric regimen (depending on the age in order to maintain or possibly reducing the body weight), the daily movement program (walking, ascending and descending stairs), the correct posture from a static and dynamic point of view, the avoidance of the prolonged orthostatism and vicious positions. One capsule was taken daily in the morning and in the evening, for a period of 3 months.

The electrotherapy procedures used were: Trabert current (fixed frequency 140 Hz, pulse duration 2ms and pause 5ms), average current frequency (frequency 80-100 Hz) for anti-inflammatory / analgesic purposes. Ultrasound was applied with the following parameters: the frequency of 1 MHz, power of 0.4W / cm<sup>2</sup>, pulsatile form, application by circular movements, using the applicator with a diameter of 5 cm and an acoustic gel, without pharmacologically active substance. The kinetic therapy methods used were static (isometric contractions, postures) and dynamic, using the elastic band to tone the quadriceps and the adductor muscles.

In the trial group, the prevalence of the knee osteoarthritis is higher in women 51.56% compared to 48.44% in men, the most affected age group being that of over 75 years with 39.06% of patients, followed by groups 55-64 and 65-74 years old in equal percentages of 30.04% (Figure 5).



**Figure 5.** Distribution of patients by sex and age group

The patients included in the group were evaluated by clinical, radiological and ultrasonographic examination at the beginning of the treatment (T1), at the end of the treatment after 15 days (T2) and at the control at 3 months (T3). They considered: spontaneous pain and mobilization, static and dynamic knee stability, muscle status, nutritional status, alignment of the lower limb segments.

From a radiological and ultrasonographic point of view, the deviations of the biomechanical axis of the lower limb segments, the narrowing of the articular space, the presence of marginal osteophytosis were pointed out.

From a functional point of view, it was considered: the pain on the visual analogue scale but also by the WOMAC scale, the functional impairment and joint pain using the WOMAC scale, the joint mobility by performing the joint balance, the quality of life of the patients by using the QOL scale.

The participants included in the study were informed and they signed the participation consent.

The recording of the data obtained in the evaluation was done in Microsoft Excel files and the mean, median, standard deviation and t-student test were used to compare the obtained results and to see if the working hypothesis was confirmed. After calculating the test t, one can appreciate the value of the index p, which shows the possibility of an existing error regarding the hypothesis.

### 3. Results and discussions

The trial confirmed the anti-inflammatory and anti-allergic role of this combination of plants, with no side effects reported during the 3 months of the trial. A comparison with a control group receiving placebo could not be made.

The pain reduction is significant especially on the VAS scale (the maximum value being 10, the minimum value being 0), the values being reduced both at the end of the treatment and at the control (Table 1). For the WOMAC scale, the reduction of pain is significant between the beginning of the

treatment and control as well as between the end of the treatment and control, but not between the beginning and the end of the treatment (absence of pain = 0, maximum pain = 4).

**Table 1.** The value of the p-index calculated on the vas and womac scales

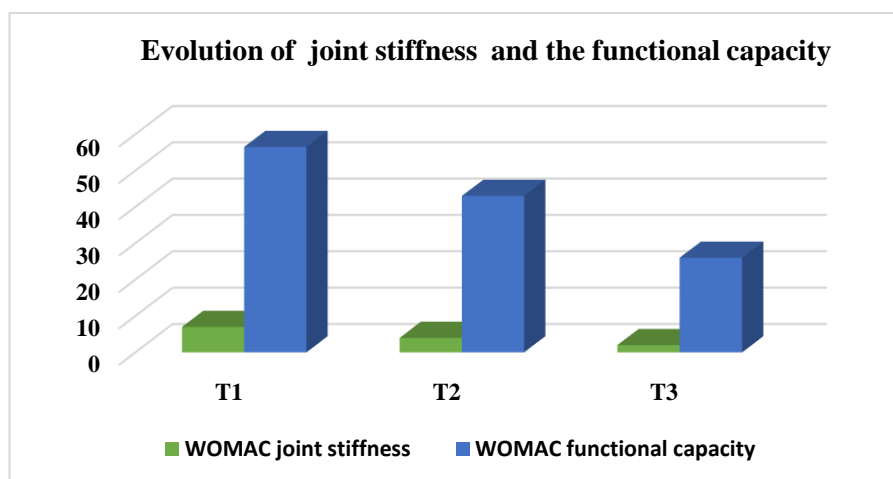
Scale	Statistics	Moment T1	Moment T2	Moment T3
VAS	Test t-student	0.0166	0.0379	0.0095
WOMAC	Test t-student	0.0291	0.0598	0.0211

The evolution of pain considered on the VAS and WOMAC scale is presented in figure 6 and the value of the p index calculated on the VAS and WOMAC scales is presented in table 1. The joint stiffness parameter decreased at all 3 moments of the evaluation (minimum value = 0, maximum value = 8)(table 2).

**Table 2.** Evolution of the joint stiffness parameter scales

Scale	Statistics	Moment T1	Moment T2	Moment T3
WOMAC	Median/ St Dev	7±0.55	4±0.47	2±0.52
WOMAC	Test t-student	0.0399	0.0645	0.0291

Significant values were also recorded in the assessment of the functional capacity that allows the daily activities to be carried out between the initial moments of the treatment and control and the completion of the treatment and control (Figure 7).



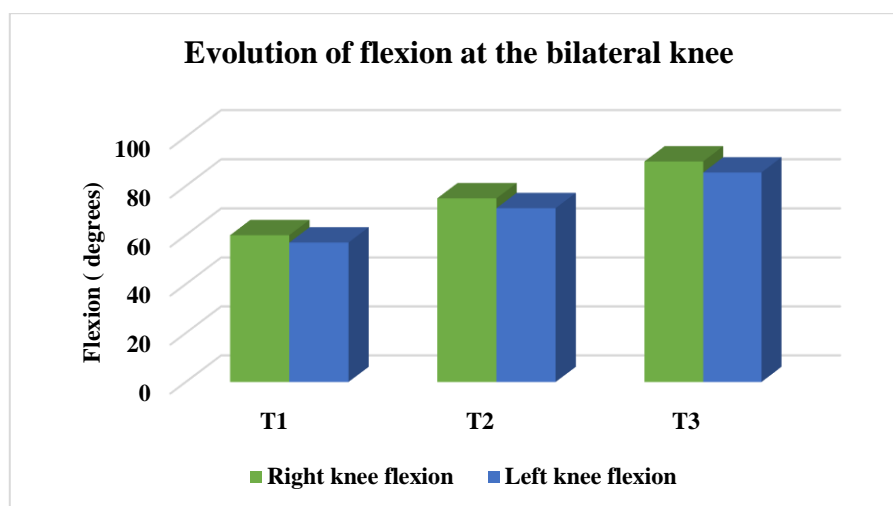
**Figure 7.** Evolution of joint stiffness and the functional capacity

Knee flexion considered with the help of goniometry improved at both knees and at all times of evaluation (Table 3) is presented in Figure 8.

**Table 3.** Evolution of flexion at the bilateral knee

Flexion	Statistics	Moment T1	Moment T2	Moment T3
Right knee	Median/Stdev	60±11.69	75±11.07	90±11.15
	Test t-std	0.0087	0.0054	0.0009
Left knee	Median/Stdev	57±14.22	71±13.21	85.5±13.54
	Test t-std	0.0095	0.0061	0.0011





**Figure 8.** Evolution of the flexion at the bilateral knee

The quality of life of elderly patients diagnosed with knee osteoarthritis was assessed by using the QOL (quality of life) scale, where the results are significant at the three evaluation times( table 4).

**Table 4.** Evolution of the quality of life parameter

SCALE	Statistics	Moment T1	Moment T2	Moment T3
WOMAC	Median/Stdev	40±4.32	60±7.54	88±11.10
WOMAC	Test t-std	0.0245	0.0222	0.0087

The complex herbal product used in the treatment of the knee osteoarthritis allowed the significant improvement of the patients' quality of life, the increase of the joint mobility, the decrease of the pain and of the inflammatory phenomena. The trials confirm the clinical efficacy of the natural anti-inflammatory with a complex composition, compared to the non-steroidal anti-inflammatories. The ingredients of this herbal product proved to be anti-inflammatory, anti-allergic, with no side effects and therapeutic safety in patients with cardiovascular disease, diabetes and gastric problems [32,33,34]. The Boswellic acids play an important role in pain management in musculoskeletal structures, proved the anti-inflammatory role by inhibiting inflammation mediators.

## 4. Conclusions

The natural anti-inflammatory with a complex composition used in the treatment of the knee osteoarthritis in the elderly patients has no side effects, showed its effectiveness in reducing pain and inflammation, increased the joint mobility and the patients' quality of life, allowing their social and family reintegration. The benefits of this natural anti-inflammatory are: it is a safe and risk-free alternative to classic non-steroidal anti-inflammatories, can be used for a long time, reduces pain and inflammation, increases the mobility and quality of life in this category of patients.

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