

ORIGINAL ARTICLE

# Pycnogenol®: supplementary management of symptomatic osteoarthritis with a patch. An observational registry study

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## ABSTRACT

**BACKGROUND:** The aim of the present observational registry study was to evaluate the efficacy of a thin polycarbonate patch of Pycnogenol® in alleviating symptoms of knee arthrosis, in comparison to the standard management usually applied to treat osteoarthritis (OA).

**METHODS:** A total of 67 subjects were included in the registry: 34 formed the control group, and 33 entered the active management group in which the Pycnogenol® patch was used. Two Pycnogenol® patches were used every day for three weeks. Each patch contains 110 mg Pycnogenol®. All patients included in this registry suffered from osteoarthritis of the knee.

**RESULTS:** Results from this study show that Pycnogenol® patch allows faster improvement in OA symptoms, with a decrease in the use of non-steroidal anti-inflammatory drugs and other painkillers. Pycnogenol® patch significantly reduced C reactive protein and ESR.

**CONCLUSIONS:** Pycnogenol® patch was effective in controlling mild to moderate pain and inflammations and its related symptoms in subjects with knee OA over a period of three weeks.

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**KEY WORDS:** Osteoarthritis, knee - Pycnogenol® - Transdermal patch - Inflammation.

Osteoarthritis (OA) is a chronic disease causing physical disability and impairing quality of life of many patients in industrialized countries as well as developing countries, with a significant impact on healthcare costs.<sup>1</sup> The few currently available treatment options for OA mainly focus on the control of symptoms; lifestyle implementations such as physical exercise and physiotherapy are also useful.<sup>2, 3</sup> Non-steroidal anti-inflammatory drugs (NSAIDs) are very commonly used to control

painful osteoarthritis attacks, although their cost is high and they are associated to significant adverse events. Thus, NSAIDs and corticosteroids are limited to severe exacerbations of OA, whereas a less aggressive therapeutic approach is widely used to manage milder episodes of the disease.<sup>4</sup>

Standardized supplements have been recently used to manage signs and symptoms of OA, in order to control both costs and occurrence and severity of side effects.<sup>1-4</sup> Subjects with known

chronic disease may significantly benefit from the use of natural standardized supplements.<sup>5-7</sup>

The standardized supplement Pycnogenol® has been already tested in several studies, and, in the setting of arthrosis, it demonstrated a significant activity both on symptoms and on objective inflammatory parameters.<sup>8-14</sup> Recently, a patch formulation of Pycnogenol® has been developed and validated for the treatment of muscular or joint pain.<sup>15, 16</sup> The aim of the present observational registry was to evaluate the efficacy of a thin polycarbonate patch of Pycnogenol® in alleviating symptoms of knee arthrosis, in comparison to the standard management usually applied to treat OA.

### Materials and methods

Registries are used to add “real-life” data to the clinical background of supplementation products.<sup>17</sup> For instance, their design is specific: patients can autonomously choose which group to enter, either the control or the active treatment group, as no predefined allocation or randomization is performed by the investigators, and the supplementation is added an open-label. To note, supplementation is administered on top of standard management, without any placebo. Follow up varies according to patients’ need and caregivers availability. Compliance to treatment, safety and tolerability are the main endpoints of these registries.

A total of 67 subjects were included in the study: 34 formed the control group, and 33 entered the active treatment group in which the Pycnogenol® patch was used.

All patients included in this registry suffered from osteoarthritis of the knee (either one or two joints), confirmed by X-ray, according to the criteria or the American College of Rheumatology.<sup>1-4</sup> All subjects were able to walk and perform all normal daily life activities.

Presence of any cardiovascular or metabolic alteration requiring pharmacological treatment, a Body Mass Index >25 kg/m<sup>2</sup>, surgery or arthroscopy within three months prior to date of registry start, oncological conditions, anemia, severe bone or joint diseases or deformation and orthopedic condition preventing patients from

walking, pregnancy, breastfeeding, and planned conception were all exclusion criteria.

In accordance with the investigators and with their own general practitioner, patients were instructed to use any temporary “on-demand” treatment they considered necessary to control their symptoms.<sup>4</sup>

All subjects were informed about the aim of this registry, and they were allowed to use NSAIDs — or any other painkiller as needed; also, they could leave the registry at any time.

The clinical evaluation comprised both subjective and objective parameters including:

- subjective level of pain scored on a visual analogue scale line (scale 1-5);
- presence of local inflammation by fast thermography and tenderness areas (score 1-5);
- thermal imaging of affected joints and peri-articular areas identified the highest temperature (in °C) by means of a FLIR 440 Thermal camera (FLIR, Sweden);
- capability of walking and standing with or without pain;
- elevation in plasma erythrocyte sedimentation rate (ESR) and C reactive protein (CRP).

Objective of the registry was to assess the reduction in the use of painkillers (mainly NSAIDs), the improvement of symptoms intensity, the reduction in medical consultations or physiotherapy within three weeks of treatment with a Pycnogenol® patch. Two Pycnogenol® patches were used every day for three weeks, applied as close as possible to the painful area. Each patch contains Pycnogenol® 110 mg, is very thin and small (57x88 mm;<1 mm), flexible, waterproof and adaptable to motion,<sup>15</sup> and with optimal skin adhesion.

### Statistical analysis

All results were analyzed by descriptive statistics. Intra- and inter-group comparisons were performed by the Student *t*-test or the ANOVA Test, as appropriate. A *p* value <0.05 was considered statistically significant. On the basis of previous observations, a group of at least 20 subjects in each group was considered necessary to evaluate the differences in the effects of management during the registry period of at least two weeks.

### Results

The SM group and the Pycnogenol® patch group were comparable for baseline characteristics (Table I). Three dropouts due to logistical problems, one in the supplementation group and two in the control group, were registered. Clinical results are shown in Table II.

Local pain decreased more significantly with Pycnogenol® patch (P<0.05). The same result was evident in terms of joint inflammation and tenderness areas (P<0.05). Thermal imaging indicated a significant decrease in the temperature of affected areas after three weeks of treatment with Pycnogenol® patch (P<0.05). Also, subjects in the active treatment group were more active and mobile than control, as their symptoms, including pain, were more controlled. The patch was therefore considered more effective than SM only (P<0.05) in highly inflamed and painful areas. After three weeks, 14/33 patients in the patch group (42.4%) were asymptomatic *versus* 8/34 subjects in the control group (23.5%).

Motion and standing dysfunctions were also significantly decreased in the patch group as compared to SM; knee swelling similarly decreased with Pycnogenol® patch more effectively than with SM only (P<0.05).

Laboratory tests revealed that normalization of ESR and C-reactive protein was greater in the patch group than in the SM only group (P<0.05). Also, the absolute average values of ESR and C-reactive protein decreased more significantly in the patch group than in controls (P<0.05).

The use of other drugs (mainly NSAIDs) after three weeks was 37.5% for patch patients *versus* 84.4% of patients in the SM group. This difference was statistically significant (P<0.05). Only 12% of patients using the patch had to consult a specialist during the three weeks of treatment as compared to 78% of the controls (P<0.05). Moreover, only 9% of patients in the Pycnogenol® group recurred to physiotherapy *vs.* 66% of patients in the group treated with SM only (P<0.05). No significant side effects or tolerability issue (*i.e.* allergic reactions or effects indicating the removal of the patch) were reported with the patch.

TABLE I.—*Details of the registry patients.*

	PP patients	Controls
Number included	33 (females 16)	34 (females 15)
Lost	1	2
Mean age; SD	43.3;4.4	42.7;2.1
Range	35-55	35-53
Days of treatment; SD	22.4;1	22.1;3
Minimum	21	21

TABLE II.—*Clinical targets.*

Clinical targets		PP patients	Controls
1 Pain score; SD (1 to 5 scale)	Inclusion 3 weeks	4.3;0.2 2,1;1.1*	4.2;0.4 3.4;1
2 Inflammation; SD (1 to 5 scale)	Inclusion 3 weeks	3.9;1 1.4;0.8*	3.8;0.6 2.3;1.3
3 Thermography (C°) area max temper; SD	Inclusion 3 weeks	37.3;1.4 34.6;1.5*	37.9;1.2 36.4;1.4
4 Walking/standing Dysfunction (1 to 5 scale); SD	Inclusion 3 weeks	4.2;0.5 2.8;1*	4.3;0.2 3.6;0.8
5 Knee swelling; SD (1 to 5 scale)	Inclusion 3 weeks	3.9;1 1.34;1.3*	3.8;0.6 1.9;2.2
6 LABS Elevation in ESR (subjects)	Inclusion 3 weeks	18/32 6/32*	17/32 13/32
ESR value; SD	Inclusion 3 weeks	23.5;2.2 15.4;1.5*	24.1;2 18.4;1.3
Subjects with elevated CRP	Inclusion 3 weeks	11/32 4/32*	10/32 7/32
CRP protein mg/L	Inclusion 3 weeks	42.2;3.1 22.3;2.2*	41.2;1.9 33;2.1
Use of other products	3 W	12/32** 37.5%**	27/32 84.4%
Consultations or physiotherapy	3W 3W	12%** 9%**	78% 66%

Scale 1-5: 1: no symptoms; 2: occasional symptom, only one limb and after work or standing or use of limb; 3: moderate symptom, requiring treatment; present most of the time; 4: symptom moderate-severe; present all time; treatment/attention required; 5: debilitating symptoms always present; subject require assistance, therapy needed. Dysfunction scale: 1: normal; 2: very minor limitation; 3: limitation in bending/stretching using the limb (bending <50% of the normal angle); 4: unable to work; 5: unable to perform any action without assistance or medications. \*P<0.05 *vs.* baseline. \*\*P<0.05 *vs.* controls.

### Discussion

Results from this registry show that Pycnogenol® patch allows faster improvement in OA symptoms, with a decrease in the use of NSAIDs and other painkillers, as opposed to SM only.

OA is characterized by a wide range of clinical manifestations, all associated to very high socio-economical costs; thus, new or alternative therapies are being widely assessed, mainly in the form of dietary supplementation. These

products may also decrease the need for medical attention, with a consequent reduction in medical costs.

Joints and associated muscular pain are particularly intense after exercise, and tend to restrain patients from moving properly and exercising,<sup>4, 15</sup> thus impairing their overall quality of life. For instance, the inability to properly use a limb may reduce the will and capacity of regular exercise, and it may become a significant, accessory, cardiovascular risk factor.<sup>12</sup> The minimal use of the affected joints and limb may also produce a significant swelling of the limb itself, due to a decreased function of the venous-muscular pump. This may turn out to be a risk condition for venous thrombosis.<sup>18, 19</sup>

Pycnogenol® has already been used in the treatment of several inflammatory conditions, with positive results. According to our data, Pycnogenol® patch is more effective than the SM only in the treatment of OA joints pain.

The lower need for additional “on-demand” drugs treatment with Pycnogenol® patch resulted in lower costs, but more importantly many possible side effects of these drugs could be prevented. Thus, the patch can be an important option for patients with painful knee OA.

The field of transdermal patches is rapidly evolving, with many new products coming on their way for use in several clinical conditions. When considering joint and muscular pain, most physical treatments may help in many cases, but they are time consuming and costly (*i.e.*, physiotherapy) and usually not reimbursed by most health care providers. Pycnogenol® is safe and effective alternative to these costly treatments, and may represent a significant self-management option.

Additionally, the observation of decreased oxidative stress levels in subjects using Pycnogenol® patch, as reported also in previous studies,<sup>16</sup> indicates that Pycnogenol® enters the bloodstream from the patch and exerts its specific activity on the inflammatory pathways that lead to increased oxidative stress.

Standardized food supplements are a significant option for self-medication, as they are safe and can be self-managed without important risks and with a great reduction in medical costs.<sup>17</sup>

## Conclusions

Pycnogenol® patch was effective in controlling mild to moderate pain and inflammations, and its related symptoms, in subjects with knee OA over a period of three weeks. Pycnogenol® patch is safe and highly tolerated, and thus it can be a significant option to avoid other expensive and potentially dangerous drugs which carry out possible serious side effects.

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*Conflicts of interest.*—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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