Influence of SYSADOA group chemicals on progression of human knee joint osteoarthritis: New objective evaluation method – measuring of rheological properties *in vivo*

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Abstract

OBJECTIVES: This study seeks to demonstrate the influence of pharmacological substances from the SYSADOA group on the progression of osteoarthritis in the human knee. The quantification methods were direct measurement of the rheological properties of the knee joints in vivo and standard WOMAC index questionnaires.

MATERIALS AND METHODS: The drugs were administered orally to 34 probands with second degree gonarthrosis for 13 weeks. The untreated control group consisted of 10 probands. The rheological properties of the joints were determined by a biorheometer, and subjective assessment of the knees by patients (WOMAC) before and after medication, and for a further 13 weeks. Changes in the calculated parameters over time were compared.

RESULTS: During the audited perioda slight deterioration in all of the parameters was observed in the untreated group. The treated group, however, improved in all the parameters and some indicators showed statistically significant differences. The positive effects of the SYSADOA persisted for 3 months after the end of treatments. Partial correlation was found between the results of the WOMAC questionnaire and the rheological measurements.

CONCLUSIONS: This study shows the positive effects of the preparation on arthritic changes in the knee joint, but due to the large variance of the collected data, this conclusion is on the borderline of statistical significance. The method of measuring the rheological properties of the joints is suitable for evaluating the progression of OA.

Abbreviations:

SYSADOA	- SYmptomatic Slow Acting Drugs for OsteoArthritis
CHS	- Chondroitin Sulphate
GS	- Glucosamine Sulphate
WOMAC	- West Ontario and McMaster Osteoarthritis Index
OA	- OsteoArthritis

O R I G I N A L   A R T I C L E

INTRODUCTION

Many professional studies have attempted to show the influence of pharmacological substances from the SYSADOA group on the progression of osteoarthritis (OA), but usually with not entirely convincing results. The main contribution of our study to a solution of this problem is the use of a unique objectification method of measurement of the rheological properties of the knee joint.

OA is a very limiting disease affecting 12–15% of the world's population, so it is one of the most common chronic disorders. The symptoms of OA can be found in up to 80% of persons older than 55 years (Felson 2000, Song 2003). OA, a form of arthritis, is an idiopathic joint disease caused by an imbalance between synthesis and degradation of articular cartilage, accompanied by fibrosis of the joint capsule, formation of osteophytes, osteosclerosis and inflammation of the synovial membrane. In the course of the disease an erosion of articular cartilage takes place, ending up in exposure of subchondral bone and disappearance of the articular fissure (Kellgren & Lawrence 1957). Clinical manifestations include stiffness or joint pain (Eustice, 2008), movement restrictions (Pavelka, 2002), instability (Hinton, 2002), crepitus, swelling (Trnava 2002), osteophytes (Moskowicz 2001), and narrowing of the articular fissure. However, because the primarily affected articular cartilage lacks innervation, the OA process does not always result in clinical manifestations (Gremion, 2009). SYSADOA substances, which include hyaluronic acid (HA), glucosamine sulphate (GS) and chondroitin sulphate (CHS), should have a positive impact on the restoration of articular cartilage, synovial fluid quality and anti-inflammatory effects. In our article we will only deal with the efficiency of CHS and GS in combination. The main expected physiological effect of GS is the inhibition of proteolytic and lysosomal enzymes and stimulation of glycosaminoglycan synthesis. CHS is the substance that is a physiological part of the articular cartilage with a positive influence on the formation of proteoglycans and collagen type II (Marek, 2005). These preparations, administered generally per os, have long-term effects. The improvement occurs 4–6 weeks after the first application and the positive effect lasts at least 2–3 months (Marek, 2005).

Professional studies, however, are only *partially* successful in providing evidence of positive effects of substances in the SYSADOA group. Positive results were obtained via meta-analysis of randomized controlled trials on the effectiveness of GS in OA therapy. Twenty randomized trials reported that GS has better effects than a placebo in the parameters of pain (28%) and the joint function parameter in the Lequesne index by 21% (Cohrane Collaboration, 2005). Two similar studies (Reginster *et al.* 2001; Pavelka *et al.* 2002) were also successful, as they independently confirmed the efficiency of GS on the symptomatology and structure of OA using the WOMAC index and measurement of the joint fissure on an X-ray. A comprehensive meta-analysis (Richy *et al.* 2003) dealt with the results of randomized controlled trials on the effects of GS and CHS on gonarthrosis between 1980 and 2002. The results showed the significant efficacy of GS and CHS in all monitored parameters. CHS's efficacy in OA of the knee was dealt with by Mazzieres *et al.* (2001) in a double-blind, randomized, placebo-controlled trial. The results showed a non-significant improvement in the group undergoing CHS therapy. A GAIT (Glucosamine/Chondroitin Arthritis Intervention Trial) compared the effectiveness of GS and CHS and their combination with a placebo in knee OA. The efficiency of GS, CHS and a combination of both, however, was about the same as the placebo group (Clegg *et al.* 2006).

All these studies, however, have only used the subjective assessment of patients using questionnaires (WOMAC, Lequesne index), or subjective physician examination, and the only objective method was the measuring of the size of the joint fissure from X-ray images (only Reginster *et al.* 2001; Pavelka *et al.* 2002). In order to objectively quantify the effects of GS and CHS substances in our combined study we used changes in rheological properties of the knee joint complex *in vivo*, and subjective evaluation by the WOMAC questionnaire method. Using a unique device – a biorheometer (Utility model-patent: PUV 2011-25188) – we made direct measurements of passive resistance to bending the knee. From the measured hysteresis curve we calculated the mechanical parameters (dissipated energy, toughness and efficiency) and compared these with the WOMAC questionnaires before and three months after the administration of the drugs, and once more after another three months. The study included 34 patients with approximately second degree gonarthrosis. The control group consisted of 10 probands with first degree arthritic changes. The tested preparation contained 500 mg of GS and 400 mg of CHS per tablet. The main objective of our study was to determine the effect of these drugs on the progression of knee joint OA, the secondary objective was an evaluation of the suitability of the objectification methods used. These objectives can be summarized into four main hypotheses:

1. The used preparation positively affects the rheological properties of the second degree OA-affected knee.
2. The used preparation positively affects the subjective symptoms in patients with second degree OA of the knee joints.
3. The positive effects of the preparation persist even after the course of treatment.
4. There is a correlation between the mechanical properties of knee joints with OA and the subjective perception of the difficulties by patients.

MATERIALS AND METHODS

The study was attended in its entirety by a total of 44 probands, divided into two groups. The descriptive characteristics of the two groups are indicated in Table 1. The first group, the "treated" group, used the manufacturer's recommended dosage of the formulation – 3 tablets orally per day (morning, noon, evening) for 13 weeks. The total daily dose was therefore 1 500 mg of GS and 1 200 mg of CHS. The group consisted of a series of patients who were diagnosed with second degree gonarthritis using X-rays and examination by a physician. Probands were not receiving any other complementary therapy, medication or rehabilitation, and it was recommended that they "carry on with life as usual". The daily activities of patients, injuries, illnesses, or use of other drugs were monitored using auxiliary questionnaires. Six probands out of the original 50 were excluded from the study due to injury, illness, or failure to comply with measuring deadlines. The "control" group consisted of 10 probands with clinical findings of first degree gonarthritis. This group did not receive any treatment or placebo, and there was therefore only measurement.

The results of the biorheometer study as well as the evaluated WOMAC questionnaires (Bellamy 2004, Olejarova 2005) confirmed the accuracy of determining the degree of osteoarthritic changes (see RESULTS). All probands signed informed consent. All measurements were performed in the BEZ laboratory at the UK FTVS under constant conditions (temperature 22±1 °C, humidity 45–55%). The comparison groups were not completely identical but in our opinion and that of the ethics committee it was not appropriate to leave patients with second degree OA without any treatment for a half year. Nonetheless, the measured data indicated that both groups were suitably comparable, even statistically. Each patient completed three test sessions during the study in 13 week intervals, within which the passive resistance of both knee joints was measured on the biorheometer and control questionnaires and WOMAC questionnaires were filled out. The first group used the tested preparation during the first 13 weeks.

The questionnaires covered basic anamnestic data (past illnesses, injuries, medication) and physical activities (sports, work, daily activities), in both the controlled period and over the course of life. Furthermore, some physiological information was measured (weight, height, dimensions of selected segments of the body) and the current device settings and data from clinical examination of the knee joints by a physiotherapist were recorded. The evaluation of these questionnaires is not part of this report, they were only used to check the suitability of probands and for the calculation and calculation of biorheometer evaluation parameters.

The WOMAC (Western Ontario and McMaster Osteoarthritis Index) clinical questionnaire test was used by patients for subjective evaluation of changes in functional disability of the knee. The questionnaire included 24 questions divided into three thematic areas – knee pain (5 questions), knee stiffness (2 questions) and everyday activities (17 questions). Completion of data by patients was performed by checking values on a five-point scale – none, mild, medium, extensive and strong problems. The questionnaires were evaluated according to the N. Bellamy method (American College of Rheumatology 2011). The scale was assigned values 0–4 and a simple sum was made of the scores of the individual subgroups. A higher score achieved thus corresponded to greater difficulties. The trend of change in subjective functional properties of the knee joint was then demonstrated by the difference in points achieved and percentage change in the score, whose significance was determined by a paired t-test after checking the normality of the distribution of the collected values. The comparison was performed between sessions 1–2, 2–3 and 1–3, except for the control group, for which questionnaires are missing from the second measurement.

Tab. 1. Descriptive characteristics of the group of probands.

	All	Men	Women	Age ave	Age min	Age max	BMI	OA degree
Group 1	34	13	21	57	40	65	28.1	2nd
Group 2	10	2	8	51	37	66	28.9	1st

For quantification of the positive impact of the preparation on knee joint arthritis we started from the basic assumption that gonarthritis causes a detectable change in the rheological properties of the joint and the preparation is capable of detectably affecting the progression of this change. Our unique laboratory device, a biorheometer, served as detector. The principle behind this measuring method is in sensing the mechanical resistance (torque) in passive (forced) movement of the knee (flexion, extension) when the muscle system of the patient is fully relaxed. Changes in the rheological properties of the joint as a whole are then evaluated, i.e. parameter changes of a "hysteresis" loop. The hysteresis loop in our case meant dependence of resistive torque [Nm] on the knee flexion angle from 10° to 90° and back. For the calculations, however, it was necessary to use angle size in arc units [rad]. This measurement method is completely painless, the knee is bent far below the physiological limit, at very slow speed of sine process (max 5°/s). The measured value – force [N]: measuring range 20 N, 1 piece 0.02 N, the relative accuracy of ±1.5%, sampling frequency 1 000 Hz, controlled variable – range of bending [°], the process of bending speed and period of measurement cycle [s]. The absolute setting error was <±2°. We defined the characteristic parameters for some pathologies (arthritis, patellar dysplasia, ACL rupture, etc.) (Kubovy & Riha 2007). For the evaluation of osteoarthritic changes 3 parameters worked best for us – dissipated energy, loss rate and dynamic stiffness, which provide an understanding of the mechanical properties of the knee as a whole – its tribology, energy efficiency and viscoelastic characteristics. The method of determination of these parameters is shown in the graph (Figure 1).

Dissipated energy in our case is the difference between mechanical energy supplied to the system and energy returned by a system. From a geometric point of view it is an area defined in the graph with a hysteresis loop, then mathematically it is the integral of the difference:

$$E_{dissip} = \int_{\alpha=0.349}^{\alpha=1.396} (M_{flex}(\alpha) - M_{ext}(\alpha))da \ ,$$

where E_{dissip} [J], is the dissipated energy, M_{flex} [Nm] and M_{ext} [Nm] are the bending momentum of the knee into flexion and extension, respectively, and α[rad] is the angle of knee flexion. Dissipated, lost energy is converted into heat in the knee, especially due to friction. Therefore we assumed that its amount is also affected by the quality of the articulating joint surfaces, i.e. properties of articular cartilage affected by gonarthritis. We therefore assumed direct influence of the quality and thickness of cartilage on the amount of the energy lost during movement of the knee, this parameter may however be affected by other factors, such as status of synovial fluids, etc.

Loser rate is a relative parameter independent of the absolute magnitudes of the bending momentum, defining energy efficiency of the knee as the accumulator of mechanical energy. Loss rate is the opposite of energy efficiency and is calculated as the ratio between lost and supplied energy:

$$\zeta = 1 - \eta = \frac{E_{dissip}}{E_{sup\square}} = \qquad ,$$

where ζ [–] is the loss rate, η [–] is the efficiency, E_{dissip} [J] and $E_{sup\square}$ [J] are dissipated and supplied energies, respectively, M^{+}_{flex} [Nm] js are positive bending momentum values in the direction of flexion and M^{-}_{ext}[Nm] are negative values of the bending momentum in the direction of extension. For the loss rate we assumed a similar dependence on the quality of the joint friction surfaces, but less influenced by the absolute value of the bending momentum, reflecting e.g. muscle or ligamentous stiffness or atrophy.

The third parameter, rigidity, is defined as the average directive of function $M_{flex}(\alpha)$ and calculated as the average of the first derivatives of this discrete function at various points depending on the angle α:

$$k = \frac{\Sigma_0^n \frac{\Delta M_{flex}(\alpha_i)}{\Delta \alpha_i}}{n} \ ,$$

where k [Nm/rad] j is the dynamic flexural stiffness, M_{flex} [Nm] is the bending momentum of the knee in flexion, α[rad] is the knee flexion angle and *n* the number of discrete points of $M_{flex}(\alpha)$ function. This characteristic is a superposition of viscoelastic properties of all compartments, but its value is affected mainly by the state of ligaments and the presence of edema in the knee joint.

Individual measurements consisted of 3+5 cycles, 3 for warm-up of the limbs and getting the examined person used to the course of the measurement. Another 5 cycles were used for evaluation. Because of the loss of information it was not possible to average individual

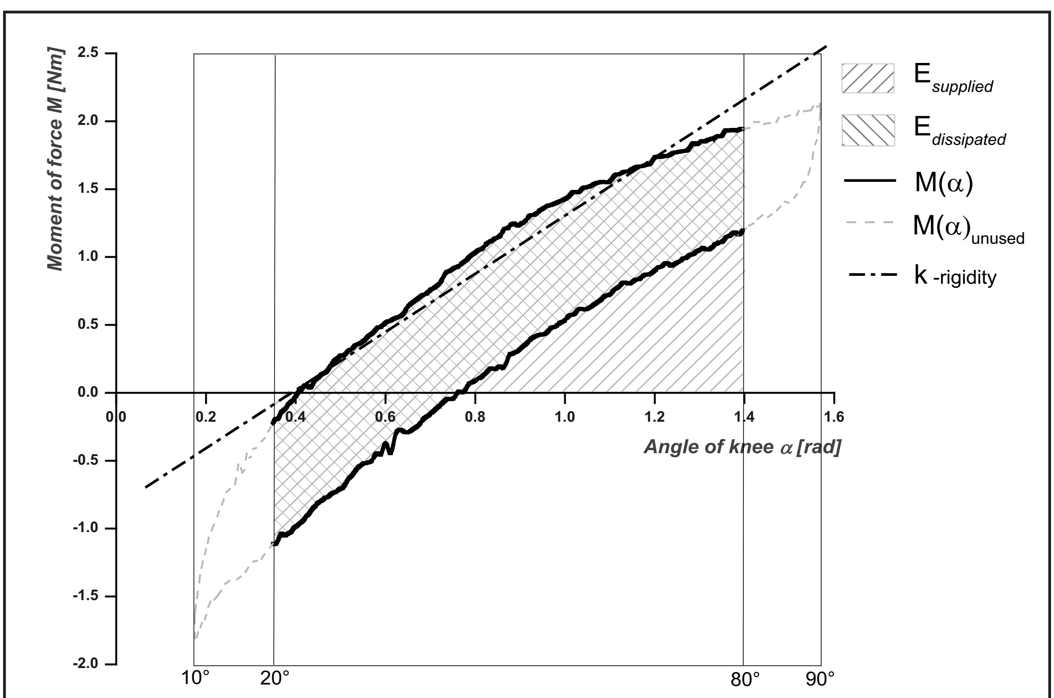

Fig. 1. Hysteresis loop of dependence of bending moment M on the angle of knee flexion α measured by a biorheometer. Only the interval α between 20° and 80° was used to calculate the parameters. The areas are indicated in the graph corresponding to the dissipated energy ($E_{dissipated}$) and supplied energy ($E_{supplied}$) for loss rate calculation and the average directive k for the calculation of stiffness.

loops, so three middle loops of the second cycle were chosen when they were in „good shape conformity“ with all the others, the parameters were separately calculated for them and then averaged. When there were larger differences between the loops caused by insufficient relaxation of the probands the measurement was repeated. All parameters were chosen in such a way that, for better orientation, it was determined that a higher value always meant worse condition.

Data obtained from WOMAC questionnaires and measured on the biorheometer were subjected to statistical analysis. Position and variability rates of individual parameters were calculated – means, medians and standard deviations and distribution normality (Kolmogorov-Smirnov) were checked. Absolute and percentage differences in the sizes of parameters were calculated, intra-individual to individual limbs in order to identify progression between the measurements. The weight of these differences was determined using the level of significance of a parametric paired t-test. Using the Pearson correlation coefficient correlations were sought between the data from the questionnaires and the data measured on the biorheometer. Finally, we also compared the treated and untreated group of probands. Data acquisitions and parameter calculations were performed using Dewesoft 7, OriginPro 8.5 and MS Excel 2010 software.

RESULTS

To confirm our hypotheses, we first compared the values of rheological and questionnaire parameters for each limb (Tables 2, 3 and Figures 2, 3). In addition we summarized the intra-individual results for individual patients (Table 4). Finally, we checked the mutual relations of rheological and subjective parameters (Tables 5, 6).

Statistical summaries of measured values for each knee and their comparison are presented in Table 2 – treated group, and Table 3 – untreated group. We calculated the absolute and percentage differences between the average values of individual measurements in both groups of probands. To check the statistical significance of achieved progression, we used a parametric paired t-test, because the distribution of measured values corresponded in most cases with normal probability distribution. The results obtained show that after a three-month course of treatment all measured parameters improved, significant differences, however, were only evident in dissipated energy, pain, stiffness of the knee and difficulties in daily activities. The knee parameters of the control (untreated) group completely deteriorated in this period, but excluding the dissipated energy parameter the deterioration was statistically insignificant (at the level of 0.05). These results therefore confirm the validity of the first and second hypothesis.

The question whether the effects of the preparation last for an extended time (3 months) after the end of treatment – Hypothesis No. 3 – cannot be clearly answered. The graph (Figure 2) clearly evidences such tendency for most parameters. After a significant improvement in the second measurement there is a slight deterioration in the third. Differences between the first and the third measurements, however, do not have statistical significance due to the large variance (Table 2). The only exception is the knee stiffness WOMAC index, where a sufficient difference persisted.

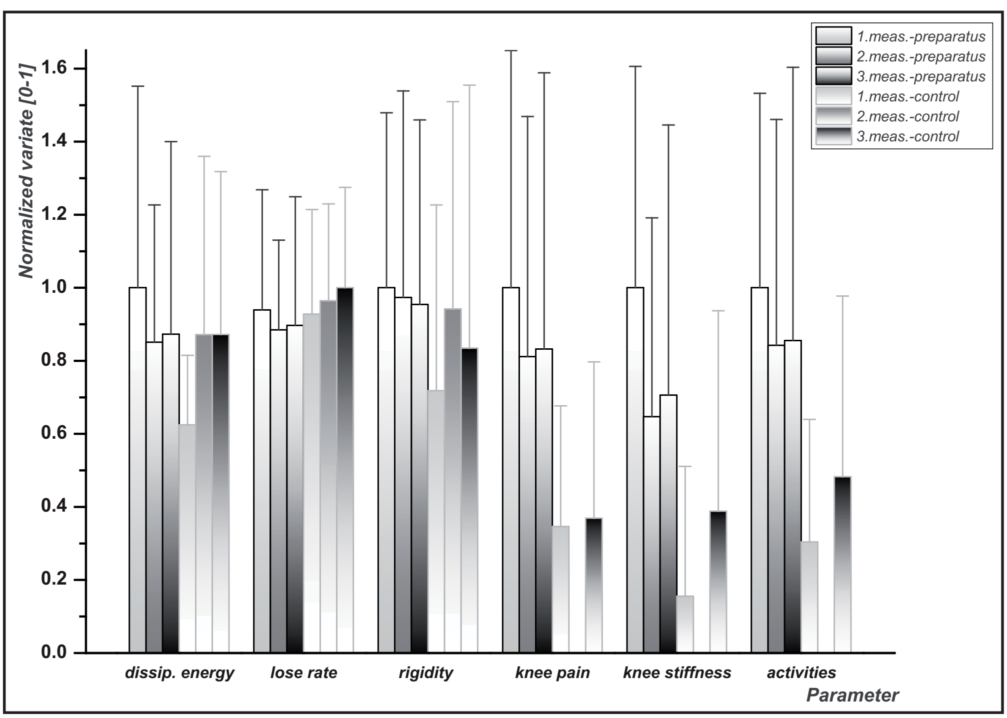

Fig. 2. Normalized graph of mean values and standard deviations of monitored parameters sorted chronologically for the 1st, 2nd and 3rd measurement (0 = 0, 1 = max achieved average parameter value). Light tops of columns are the results of the treated group, dark of the untreated.

Tab. 2. A summary of calculated parameters of hysteresis loops (biorheometer) and subjective symptoms (WOMAC) in the group of patients using the tested preparation. The negative value of the differences between measurements always means improvement, positive values mean deterioration in the knee joint.

	PREPARATION GROUP BIORHEOMETER									PREPARATION GROUP WOMAC								
	dissipated energy [J]			lose rate [–]			rigidity [Nm/rad]			knee pain			knee stiffness			everyday activities		
measur.	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
sum	94.0	80.0	82.0	39.0	36.8	37.3	161.7	157.4	154.3	143.0	116.0	119.0	85.0	55.0	60.0	684.0	576.0	585.0
mean	1.382	1.176	1.206	0.574	0.541	0.548	2.379	2.315	2.269	4.3	3.5	3.6	2.6	1.7	1.8	20.7	17.5	17.7
max	3.904	2.440	4.298	0.984	0.898	0.994	4.892	6.238	6.281	13.0	11.0	13.0	6.0	6.0	9.0	42.0	54.0	69.0
min	0.151	0.289	0.000	0.112	0.287	0.000	0.113	0.024	0.000	1.0	0.0	0.0	0.0	0.0	0.0	4.0	2.0	0.0
median	1.286	1.091	1.085	0.527	0.515	0.557	2.373	2.068	2.076	4.0	2.5	2.5	2.0	2.0	1.5	20.0	13.5	12.5
SE	0.763	0.520	0.729	0.201	0.150	0.215	1.139	1.346	1.203	2.8	2.9	3.3	1.6	1.4	1.9	11.0	12.8	15.5
diff. of measur.	1–2	2–3	1–3	1–2	2–3	1–3	1–2	2–3	1–3	1–2	2–3	1–3	1–2	2–3	1–3	1–2	2–3	1–3
mean difference	–0.206	0.030	–0.176	–0.034	0.008	–0.026	–0.063	–0.046	–0.109	–0.8	0.1	–0.7	–0.9	0.2	–0.8	–3.3	0.3	–3.0
percent difference	–14.9	2.2	–12.7	–5.8	1.3	–4.5	–2.7	–1.9	–4.6	–18.9	2.1	–16.8	–35.3	5.9	–29.4	–15.8	1.3	–14.5
test of normality	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	yes	yes	no
pair t-test prob.	0.029	0.724	0.134	0.174	0.758	0.402	0.677	0.745 .	0.474	0.052	0.734	0.133	0.000	0.248	0.011	0.011	0.720	0.064

Tab. 3. A summary of calculated parameters of hysteresis loops (biorheometer) and subjective symptoms (WOMAC) in the group of patients without any treatment. The negative value of the differences between measurements always means improvement, positive values mean deterioration in the knee joint. Data from the second measurement questionnaires were unfortunately lost.

	CONTROL GROUP BIORHEOMETER									CONTROL GROUP WOMAC								
	dissipated energy [J]			lose rate [–]			rigidity [Nm/rad]			knee pain			knee stiffness			everyday activities		
measur.	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
sum	17.3	24.1	24.1	11.3	11.8	12.2	34.2	44.8	39.7	30.0		32.0	8.0		20.0	126.0		200.0
mean	0.863	1.205	1.206	0.567	0.590	0.611	1.708	2.241	1.985	1.5		1.6	0.4		1.0	6.3		10.0
max	1.332	3.397	2.780	0.965	1.000	0.906	4.696	5.395	7.588	4.0		5.0	3.0		4.0	21.0		27.0
min	0.440	0.501	0.402	0.211	0.301	0.215	–0.324	0.103	–2.150	0.0		0.0	0.0		0.0	0.0		0.0
median	0.813	1.076	1.030	0.546	0.558	0.615	1.685	2.258	1.953	1.0		1.0	0.0		0.0	3.0		8.0
SE	0.263	0.675	0.617	0.175	0.162	0.168	1.210	1.350	1.713	1.4		1.9	0.9		1.4	7.0		10.3
diff. of measur.	1–2	2–3	1–3	1–2	2–3	1–3	1–2	2–3	1–3	1–2	2–3	1–3	1–2	2–3	1–3	1–2	2–3	1–3
mean difference	0.342	0.001	0.342	0.022	0.022	0.044	0.533	–0.255	0.277			0.1			0.6			3.7
percent difference	39.6	0.1	39.7	3.9	3.9	7.8	31.2	–14.9	16.2			6.7			150.0			58.7
test of normality	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes		yes	no		no	yes		yes
pair t-test prob.	0.020	0.996	0.019	0.629	0.432	0.288	0.082	0.490	0.311			0.836			0.069			0.103

Tab. 4. Progression of probands knee status during six-month interval.

	BIORHEOMETER						WOMAC						ALTOGETHER					
	dissip. energy [%]		lose rate [%]		rigidity [%]		knee pain [%]		knee stiffness [%]		activities [%]		BIORHEOMETER [%]		WOMAC [%]		ALTOGETHER [%]	
Group	P	C	P	C	P	C	P	C	P	C	P	C	P	C	P	C	P	C
Improvement	38	20	29	30	44	20	53	30	59	10	65	40	21	0	53	40	18	0
Ambivalence	50	40	59	40	32	40	15	30	15	60	6	30	76	90	38	50	82	100
Deterioration	12	40	12	30	24	40	32	40	26	30	29	30	3	10	9	10	0	0

P - PREPARAT.; C - CONTROL

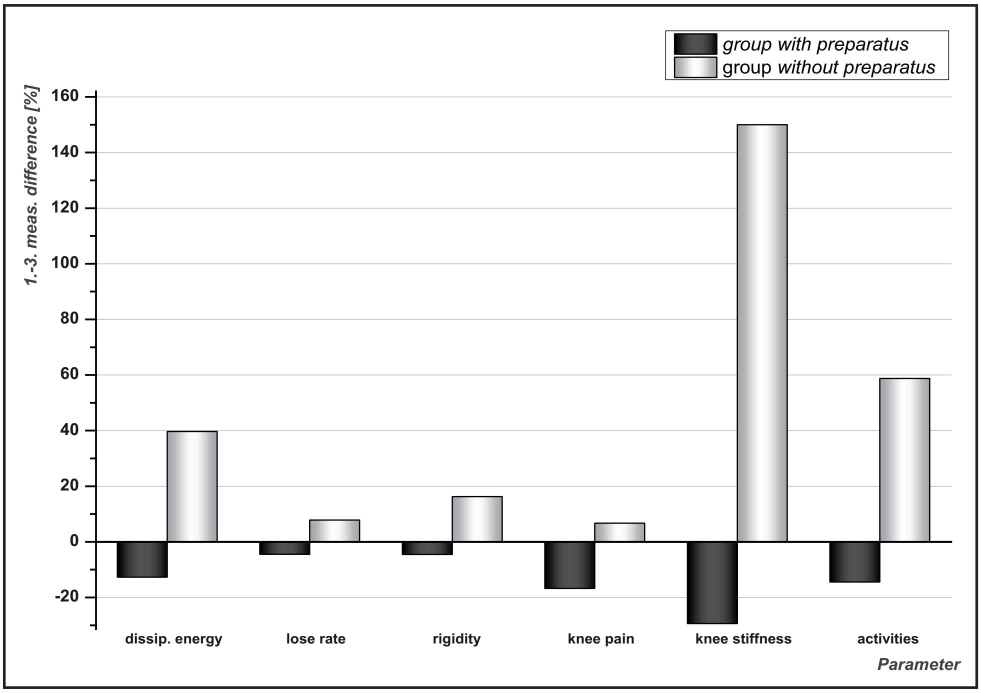

Fig. 3. Graph of percentage differences of evaluation parameters between 1st and 3rd measurement. Positive values of the light control group indicate deterioration in the knee status in all aspects, as opposed to the dark treated group.

In the untreated group a deterioration of generally all indicators took place within six months, but only achieved a significant level for dissipated energy. This chart also demonstrates the accuracy of grouping the patients according to degree of osteoarthritic changes and suitability of selected objectification parameters. The control group of patients with only first degree OA achieved significantly better results in the first measurement than probands with second degree OA and later medication. The graph also shows a lower dispersion of rheological parameter values than the subjective questionnaire method.

Differences in the progression of arthritic knee conditions between the treated and control group in the six-month period is shown in the graph (Figure 3). While the control group experienced a significant percentage deterioration in all indicators, the treated group always improved slightly. These results are, however, due to the large parameter value scattering and a limited number of probands on the border of statistical significance.

A summary of the gonarthritis development in the monitored period for each patient is in Table 4. We are talking about the differences between the 1st and 3rd measurement, i.e. the change in knee joint status during 26 weeks. This number is always a percentage of probands in the group who experienced improvement or deterioration in both or at least one of their limbs while the other remained unchanged. In the ALTOGETHER part all six parameters had to have improved/deteriorated. All those whose one leg worsened and one improved, or whose parameters did not reach more than three percent difference fell into the AMBIVALENCE category. The group taking the preparation again achieved better results in all respects. Perhaps the most significant fact is that a full 18 percent of patients using the preparation improved in all factors, which means that there were positive changes in all measured parameters of both their knees with both methods –

Tab. 5. Correlation coefficients and their significance levels between the measured mechanical properties of the knee joint and subjective difficulties of the patients.

		PAIN	STIFFNESS	ACTIVITIES
DISSIPATED ENERGY	Pearson Corr.	0.04	−0.05	−0.08
	Signification	0.573	0.410	0.198
LOSE RATE	Pearson Corr.	0.00	−0.01	−0.11
	Signification	0.992	0.934	0.092
RIGIDITY	Pearson Corr.	0.24	0.04	0.20
	Signification	0.000	0.566	0.001

Tab. 6. Correlation coefficients and their significance levels between changes in the mechanical properties of the knee joint and the changing perception of difficulties by the patients.

		PAIN	STIFFNESS	ACTIVITIES
DISSIPATED ENERGY	Pearson Corr.	0.25	0.11	0.08
	Signification	0.000	0.110	0.213
LOSE RATE	Pearson Corr.	0.15	0.10	0.06
	Signification	0.021	0.153	0.394
RIGIDITY	Pearson Corr.	0.18	−0.03	−0.02
	Signification	0.007	0.617	0.814

biorheometer and WOMAC. In the control group, no such patient was found. These results therefore again agree with hypotheses 1, 2 and 3.

The central question of the entire study was the compatibility of the results of objective measurements on the biorheometer and subjective knee evaluation by patients. Part of the answer may be the interdependence of the values obtained by individual methods. Tables 5 and 6 show the correlation coefficients (Pearson) and their levels of significance between the parameters. Table 5 contains the relationship between the parameter values of all measurements throughout the study. Table 6 contains the interdependence between the size changes of these indicators. The tables show that only rheological knee stiffness with pain and perceived difficulty in daily activities exhibits a good positive correlation of parameters. Pain in the knee is then directly proportional in the progression values to all the parameters of hysteresis loops. Also in Figure 2, we can observe the similarity of time course of the average values of the biorheometer and WOMAC parameters, especially in the group with the preparation. Hypothesis No. 4 can thus only be partially confirmed, since the statistical relevance of the results is again reduced by the large variance of the collected data.

DISCUSSION

Hypothesis No. 1, stating that the preparation positively influences the rheological properties of the second degree OA affected knee, has been demonstrated. After three months of taking 1 500 mg of GS and 1 200 mg of CHS daily the average of all three biomechanical parameters measured on the biorheometer improved among 34 probands (64 limbs). Statistical significance, however, was only achieved by the difference in energy dissipation in the joint during movement (Table 2). In contrast, in the untreated control group of 10 probands with first degree knee OA all the criteria worsened in this time interval, although again only dissipated energy (Table 3) was significant. In 21% of patients the preparation improved the rheological properties of at least one knee, the other remained unchanged at least and the condition of both knees of only one patient worsened. In the control group there was no such improvement of any patient (Table 4).

Hypothesis No. 2, that the preparation positively affects subjective symptoms in patients with second degree OA of knee joints, is also confirmed. In all three parts of the WOMAC questionnaire (knee pain, knee stiffness, daily activities) a significant improvement was shown, while the control group always showed a slight decrease (Tables 2, 3). The results of the questionnaire method, however, are not as clear-cut as it might seem from the average values of the parameters, because 40% of probands in the control group stated the overall improvement of the knee status, which is not such a significant difference in comparison with 53% of the treated group. Only 10% of patients of both groups stated overall deterioration (Table 4).

Hypothesis No. 3, that the positive effects of the preparation continue for a long time after the course of treatment has not been significantly proven. Over the three months after medication there was only a slight deterioration in all measured parameters, however, the differences between measurements 1 and 3 were no longer statistically significant (Tables 2, 3). A question also remains about the progression of the knee joints status. The fact is that a full 18 percent of patients improved in all factors while using the preparation, which means that there were positive changes in all measured parameters of both their knees by both methods (Table 4). The proof of validity of the study is in the fact that in both the methods used, the condition of both knees had a similar time course. The treated group experienced a significant improvement at first and then a slight deterioration. The control group instead continuously deteriorated.

Hypothesis No. 4, that there is a dependence between the mechanical properties of knee joints with OA and subjective perception of the difficulties by patients was confirmed only for certain parameters. Of all the indicators we can only highlight the direct proportionality between the change in the amount of dissipated energy in the knee joint and the change in knee pain, because only in these parameters did a statistically significant change occur during the study (Tables 2–4).

CONCLUSION

The study demonstrated the positive effects of the preparation on arthritic changes in the knee joint, but due to the large scattering of measured and collected data, this conclusion is on the borderline of statistical significance. The results further show that there was a significant difference in the progression of the disease symptoms between treated and control groups in the monitored six-month period. A clear correlation between objective biorheometer measurements and the subjective WOMAC questionnaire method only showed itself in the progression of the individual parameters. A significant correlation of the original data was only found between the parameters of the hysteresis curves and the knee pain index of the WOMAC questionnaires. An important finding of the study is the evidence of the biorheometer measurements' appropriateness for the determination of the progression of osteoarthritis. However, to confirm the validity of the results it is necessary to increase the number of probands, especially the control group, as the variability among living creatures is always very high.

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