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A study on healthy volunteers to assess the distribution of chondroitin sulfate in the human body immediately after taking one dose and after taking a dose every day for 14 days

Submission date
13/06/2022

Recruitment status
No longer recruiting

Registration date
22/06/2022

Overall study status
Completed

Last Edited
01/07/2022

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Chondroitin sulfate has proven to be a valuable therapeutic tool for the symptomatic treatment of osteoarthritis (OA). Condrosulf® is an oral pharmacological formulation containing chondroitin sulfate, able to alleviate the painful symptoms and the functional impairment caused by the pathological condition.

The clinical studies on Condrosulf® demonstrated effective mitigation of pain in patients with OA, particularly in the knee, the hip, and the hand. The safety profile of Condrosulf® is confirmed by the post-marketing experience worldwide. Chondroitin sulfate has been commercialized since 1983. This long experience on the market (around 40 years) confirms the safety of the product. The present study is designed to investigate the activity in the body (pharmacokinetics) of chondroitin sulfate and in blood plasma and urine samples of healthy male and female volunteers after administration of Condrosulf® single and multiple doses.

The study will add new data about the pharmacokinetics of all the mentioned analytes after a treatment of 2 weeks with the investigational medicinal product, in conditions similar to those of real product use in the target population and according to the 800 mg once-a-day dose recommended for Condrosulf®.

Who can participate?
Healthy volunteers aged between 30 and 65 years inclusive

What does the study involve?
All the study subjects will receive the same treatment, i.e. 800 mg Condrosulf® (one tablet) once a day for 14 consecutive days, i.e. from Day 1 (first dose) to Day 14 (last dose). Intervals between 2 consecutive doses will be approximately 24 h. The investigational product will be administered at the Phase I Unit at 08:00±1h on Days 1, 2, 3, 6, 9, 12, 13 and 14. Administrations at the clinic will be performed at 08:00±1 h, with 240 ml of still water, under fasting conditions on Days 1 and

14, and before breakfast on the other days. On Days 4, 5, 7, 8, 10 and 11, the study subjects will self-administer the investigational medicinal product at home following the same dose regimen (i.e. one tablet each day at 08:00±1.5 h before breakfast) with approximately 240 ml (one glass) of still water.

What are the possible benefits and risks of participating?
On the basis of chondroitin sulfate safety profile, no potential risks are foreseen for the subjects enrolled in the present study. No potential benefits are foreseen to volunteers participating in the current study.

Where is the study run from?
CROSS Research SA Phase I unit Clinical Centre (Switzerland)

When is the study starting and how long is it expected to run for?
May 2021 to July 2021

Who is funding the study?
IBSA Institut Biochimique SA (Switzerland)

Who is the main contact?
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Principal investigator

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Additional identifiers

Protocol serial number
CRO-PK-21-353, 20CH-Ct05

Study information

Scientific Title
Pharmacokinetics and safety study of Condrosulf® 800 mg tablets after single and multiple doses in healthy male and female volunteers.

Study objectives
Evaluation of pharmacokinetics and safety of chondroitin sulfate after single and multiple doses of chondroitin sulfate 800 mg tablets (Condrosulf®), administered to healthy volunteers

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/06/2021, Ethics Committee of Canton Ticino (Ufficio di sanità, Via Orico 5, 6501 Bellinzona, Switzerland; +41 (0)91 814 30 57; beatrice.giberti-gai@ti.ch), ref: 2021-01143 CE3891

Primary study design
Interventional

Study design
Single-dose multiple-dose single-center open-label pharmacokinetics safety study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Osteoarthritis

Interventions
1. Subjects receive 800 mg Condrosulf® (one tablet) once a day for 14 consecutive days, i.e. from Day 1 (first dose) to Day 14 (last dose). Intervals between 2 consecutive doses (τ) will be approximately 24 hours.
2. The investigational product will be administered at the Phase I Unit on days 1, 2, 3, 6, 9, 12, 13 and 14. Administrations at the clinic will be performed at 08:00±1 h, with 240 ml of still water, under fasting conditions on Days 1 and 14, and before breakfast on the other days.
3. On Days 4, 5, 7, 8, 10 and 11 subjects will self-administer the investigational medicinal product at home following the same dose regimen (i.e. one tablet each day at 08:00±1.5 h before breakfast) with approximately 240 ml (one glass) of still water.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Chondroitin sulfate

Primary outcome(s)
1. Pharmacokinetics (PK) of total chondroitin sulfate and of ΔDi-4S, ΔDi-0S and ΔDi-6S disaccharides measured using Baseline-corrected Cmax, AUC0-24, AUC0-t, tmax, AUC0-∞, t1/2 after administration of single (Day 1) and using Baseline-corrected Cssmax, tssmax, Cssmin, Cssave, PTF% and AUCsst after multiple doses (Day 14) of Condrosulf®
2. Baseline blood concentration values for the 3 ΔDi-4S, ΔDi-0S and ΔDi-6S disaccharides will be calculated as the arithmetic mean of the 7 pre-dose concentrations, measured on Days -2, -1 and 1. Baseline-corrected plasma concentrations will be calculated by subtracting the mean baseline value from each post-dose value, separately for each disaccharide. Total chondroitin sulfate concentrations will be calculated as the sum of baseline-corrected ΔDi-4S, ΔDi-0S, and ΔDi-6S disaccharides concentrations. PK parameters of the 3 disaccharides will be calculated from baseline-corrected concentrations.
3. The following PK parameters will be measured and/or calculated for baseline-corrected ΔDi-6S, ΔDi-4S, ΔDi-0S and total chondroitin sulfate, after a single dose (day 1) using the validated software PhoenixWinNonlin® version 6.3: Cmax, tmax, λz, t1/2, AUC0-t, AUC0-24, AUC0-∞, % AUCextra, Ae0-t Fe0-t
4. The following PK parameters will be measured and/or calculated for baseline-corrected ΔDi-6S, ΔDi-4S, ΔDi-0S, and total chondroitin sulfate, using the same software, after multiple doses (Day 14) of the IMP: Cssmax, tssmax, Cssmin, Cssave, AUCsst, PTF%, Aesst

Key secondary outcome(s)
1. Urinary excretion of total chondroitin sulfate and of ΔDi-4S, ΔDi-0S and ΔDi-6S disaccharides measured using Baseline-corrected Ae0-t, Fe0-t and Clr after single dose (Day 1) of the investigational medicinal and using Baseline-corrected Aesst after multiple doses (Day 14) of

Condrosulf®
Baseline-corrected urine values for the 3 ΔDi-4S, ΔDi-0S and ΔDi-6S disaccharides will be measured at pre-dose on Day 1.
Baseline-corrected urine concentrations will be calculated by subtracting the baseline value (Day 1 pre-dose) from each post-dose interval value, separately for each disaccharide.
Negative baseline-corrected concentrations values, if present, will be considered as 0.
Total chondroitin sulfate concentrations will be calculated as the sum of baseline-corrected ΔDi-4S, ΔDi-0S and ΔDi-6S disaccharides concentrations.
PK parameters of the 3 disaccharides will be calculated from baseline-corrected concentrations.
All PK parameters are measured and/or calculated for baseline-corrected ΔDi- 6S, ΔDi-4S, ΔDi-0S and total chondroitin sulfate, using the validated software Phoenix WinNonlin® version 6.3

2. Evaluation of the safety and tolerability of Condrosulf® based on:
2.1. The incidence of treatment-emergent adverse events collected throughout the study
2.2. Vital signs (blood pressure, heart rate), physical examinations, body weight, ECG and laboratory parameters collected at the following timepoints:
2.2.1. Blood pressure, heart rate (measured after 5 min at rest in the sitting position): at Screening, on Day -3, on Days 1-2 at pre-dose, 3, 12, 24 h post-dose. On Days 14-15 at pre-dose, 3, 12, 24, 36 h postdose. On Days 3, 6, 9 at pre-dose. On day 16 at 48 h post-dose. At ETV (if applicable).
2.2.2 Physical examinations (overall Investigator's interpretation and clinically significant abnormalities): performed at the screening and final visit/ETV
2.2.3. Body weight: at screening and final visit/ETV
2.2.4. ECG (12-Leads ECGs will be performed in supine position): at Screening, on Day 2 at 24 h post-dose; on day 16 at 48 h post-dose. At ETV (if applicable).
2.2.5. Laboratory parameters: at screening and final visit/ETV. The following laboratory analyses were performed:
2.2.5.1. Hematology (Leukocytes and leukocyte differential count, erythrocytes, hemoglobin, hematocrit, MCV, MCH, MCHC, thrombocytes)
2.2.5.2. Blood chemistry
2.2.5.3. Electrolytes (sodium, potassium, calcium, chloride, inorganic phosphorus)
2.2.5.4. Enzymes (alkaline phosphatase, γ-GT, AST, ALT)
2.2.5.5. Substrates/metabolites (total bilirubin, creatinine, glucose, urea, uric acid, total cholesterol, triglycerides)
2.2.5.6. Proteins (total proteins)
2.2.5.7. Serum virology: Hepatitis B (HBs antigen), Hepatitis C (HCV antibodies), HIV 1/2 (HIV Ag /Ab combo).
2.2.5.8. Urine analysis: Urine chemical analysis – stick (pH, specific weight, appearance, color, nitrites, proteins, glucose, urobilinogen, bilirubin, ketones, hematic pigments, leukocytes) and Urine sediment - analysis performed only if positive (leukocytes, erythrocytes, flat cells, round cells, crystals, cylinders, mucus, bacteria)

Completion date
30/07/2021

Eligibility

Key inclusion criteria
1. Signed written informed consent before inclusion in the study
2. Men or women aged between 30 and 65 years old inclusive
3. Body Mass Index between 18.5 and 30 kg/m2 inclusive

4. Vital signs measured after 5 min at rest in the sitting position:
4.1. Systolic blood pressure (SBP) 100-139 mmHg
4.2. Diastolic blood pressure (DBP) 50-89 mmHg
4.3. Heart rate 50-90 bpm,
5. Able to comprehend the full nature and purpose of the study, including possible risks and side effects; ability to co-operate with the Investigator and to comply with the requirements of the entire study
6. Women of child-bearing potential must be using at least one of the following reliable methods of contraception:
6.1. Hormonal oral, implantable, transdermal, or injectable contraceptives for at least 2 months before the screening visit
6.2. A non-hormonal intrauterine device (IUD) or female condom with spermicide or contraceptive sponge with spermicide or diaphragm with spermicide or cervical cap with spermicide for at least 2 months before the screening visit
6.3. A male sexual partner who agrees to use a male condom with spermicide
6.4. A sterile sexual partner
7. Women of non-child-bearing potential or in post-menopausal status for at least 1 year will be admitted
8. For all women, pregnancy test results must be negative at screening

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
18

Key exclusion criteria
1. Clinically significant abnormalities on 12-leads (supine position) electrocardiogram (ECG)
2. Clinically significant abnormal physical findings which could interfere with the objectives of the study
3. Clinically significant abnormal laboratory values indicative of physical illness
4. Known or presumed hypersensitivity to the active principle (chondroitin sulfate) and/or formulations' ingredients; history of anaphylaxis to drugs or allergic reactions in general, which the Investigator considers may affect the outcome of the study
5. Significant history of renal, hepatic, gastrointestinal, cardiovascular, respiratory, skin, hematological, endocrine or neurological diseases that may interfere with the aim of the study
6. Medications, including over-the-counter (OTC) medications, herbal remedies, and food supplements containing chondroitin sulfate for 2 weeks before the start of the study
7. Participation in the evaluation of any investigational product for 3 months before this study.

The 3-month interval is calculated as the time between the first calendar day of the month that follows the last visit of the previous study and the first day of the present study
8. Blood donation for 3 months before this study
9. History of drugs, alcohol (>1 drink/day for women and >2 drinks/day for men, defined according to the USDA Dietary Guidelines 2020-2025), caffeine (>5 cups coffee/tea/day) or tobacco abuse (≥10 cigarettes/day)
10. Positive result at the drug test at screening or day-3
11. Positive alcohol breath test on day -3
12. Abnormal diets (<1600 or >3500 kcal/day) or substantial changes in eating habits in the 4 weeks before this study; vegetarians
13. Positive or missing pregnancy test at screening or day -3, pregnant or lactating women

Date of first enrolment
05/07/2021

Date of final enrolment
07/07/2021

Locations

Countries of recruitment
Switzerland

Study participating centre
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Sponsor information

Organisation
IBSA Institut Biochimique (Switzerland)

ROR
https://ror.org/051tj3a26

Funder(s)

Funder type
Industry

Funder Name
IBSA Institut Biochimique

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		01/07/2022	01/07/2022	No	No