A Clinical Study on Bovine Bone Collagen Peptide in the Management of Knee Joint Osteoarthritis

By **Auroville Health Care**, Chennai, India

Sponsored by **Nitta Gelatin India Limited**, Kochi, India

Study Title

A double - blind, placebo-controlled, randomized trial to determine the effectiveness and safety of bovine bone collagen peptide as add-on nutritional supplement in management of subjects with knee joint osteoarthritis

Objectives

Primary:

To determine that Bovine Bone Collagen Peptide can limit the structural disease progression while providing the symptomatic benefit in subjects with knee joint Osteoarthritis in comparison with placebo.

Secondary:

To confirm the overall safety of Bovine Bone Collagen Peptide in subjects with knee joint Osteoarthritis

Approvals

- DCGI Notification
- National Ethics Committee (Independent Ethics Committee)
- Ethics committee - Apollo Hospital (Institutional Ethics Committee)

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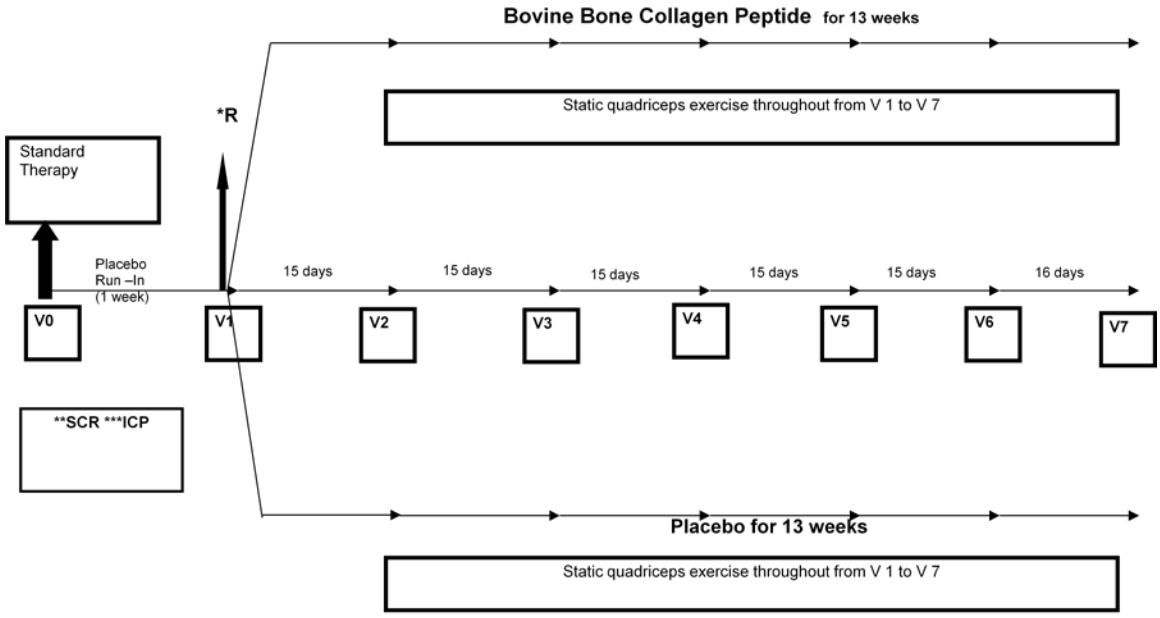
Compliance

- Trial was conducted in compliance with the protocol, and the applicable regulatory requirements:
  - Principles stated in Declaration of Helsinki.
  - International Conference on Harmonization Good Clinical Practice E6 (ICHGCP).
  - Schedule – Y: DRUGS AND COSMETICS (II AMENDMENT) RULES, 2005
- Trial was registered in CTRI web site as per the directions of DCGI, India.

Study Design

No. of subjects (planned)	20 subjects with BBCP(Bovine Bone Collagen Peptide) + 10 subjects with Placebo
Number of subjects (analyzed)	PP : 18 subjects with BBCP + 10 subjects with placebo ITT : 20subjects with BBCP + 10 subjects with placebo[Including two dropouts]
Dosage (Collagen Peptide)	10 gm/day (5 gm BID) dissolved either in 250 ml water or milk.
Dosage (Placebo - Maltodextrin)	10 gm/day (5 gm BID) dissolved either in 250 ml water or milk.
Route of Administration	Oral
Treatment Duration	13 Weeks (91 days)

Study design – Schematic



*R – Randomization; **SCR – Screening; ***ICP – Informed Consent Process

Study Endpoints

Outcome Measures

- **WOMAC Score Analysis**
  - The WOMAC (Western Ontario and Mc Master Universities) index is a disease specific self administered health measure. It is used to monitor the course of disease or to determine the effectiveness of medication for Osteoarthritis.

- **VAS Score Analysis**
  - VAS (Visual Analogue Scale) is a pain measurement scale used for assessing drug efficacy and patient progress in Osteoarthritis.

- **QoL Score Analysis (WOMAC + VAS)**
  - QoL is the summation of WOMAC and VAS scores that indicates improvements in overall quality of life in patients with Osteoarthritis in terms of reduced pain during ADL

- **X ray Analysis**
  - Kellegren Lawrence Grading of Knee Joint Osteoarthritis

Efficacy Endpoints

- **Primary Efficacy End Points**
  - WOMAC score - reduction in score by ≥ 20 points from baseline to visit 7.
  - VAS pain score - reduction in score by ≥ 4 points from baseline to visit 7.
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- **Secondary Efficacy End Point**
  - WOMAC score - reduction in score by ≥ 10 points from baseline to visit 7.
  - VAS pain score - reduction in score by ≥ 2 points from baseline to visit 7.
  - X-ray - remission in grade levels.
  - QOL –reduction in score by ≥ 20 points from baseline to visit 7.

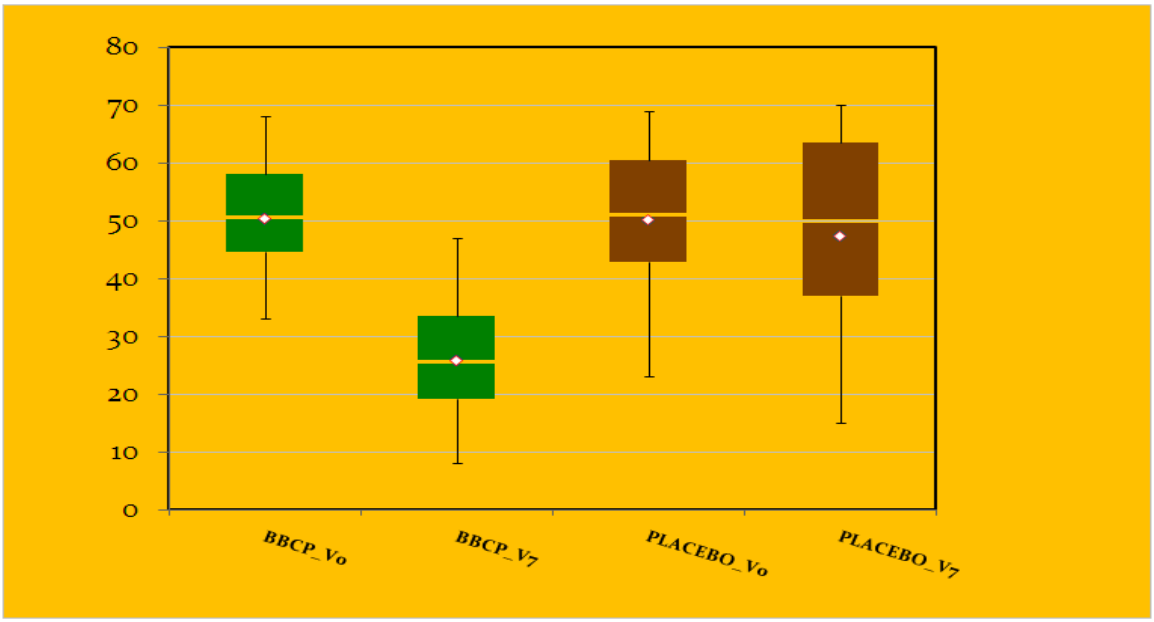
Safety Endpoints

- Occurrence of any adverse events.
- Significant changes in laboratory values, vital signs, physical functions

Statistical Methods for End Point Analysis

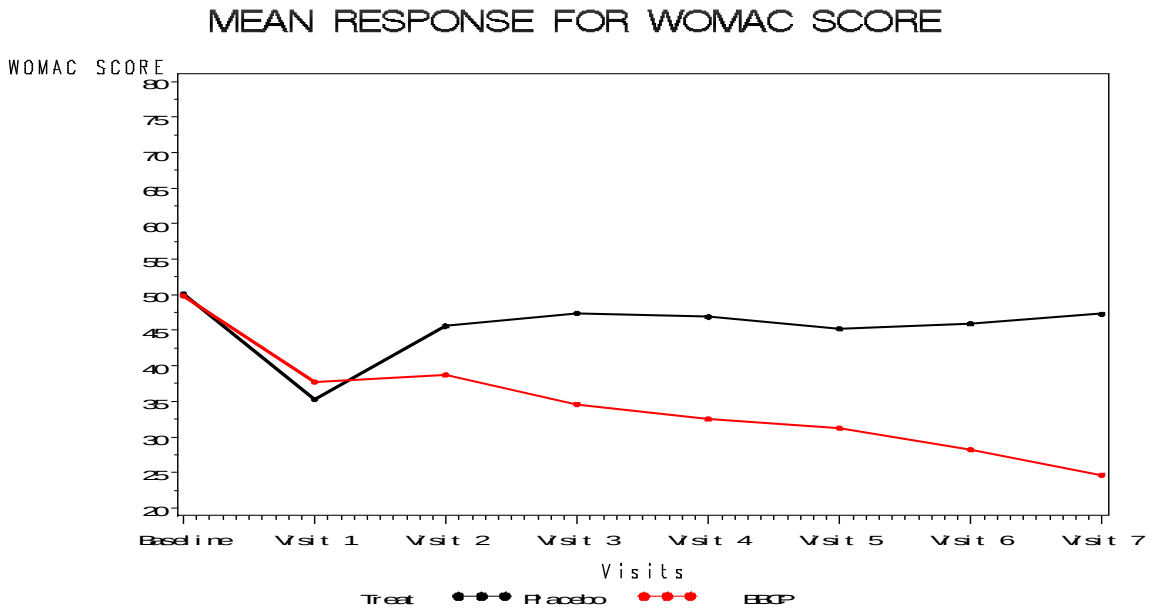
WOMAC Score Analysis

Box & Whisker Plot for WOMAC Score between Baseline & Visit 7



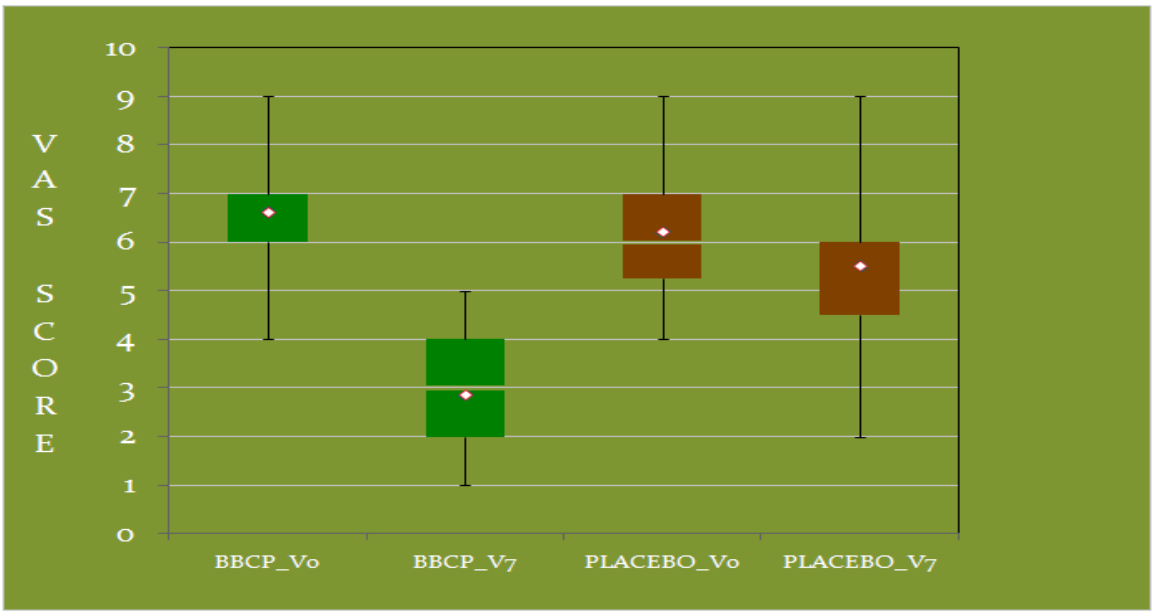
Out of 18 subjects receiving BBCP 14 (77.7%) subjects had shown good to better improvement in WOMAC score.

Statistically significant changes (p = 0.0001) were observed between groups BBCP and Placebo.



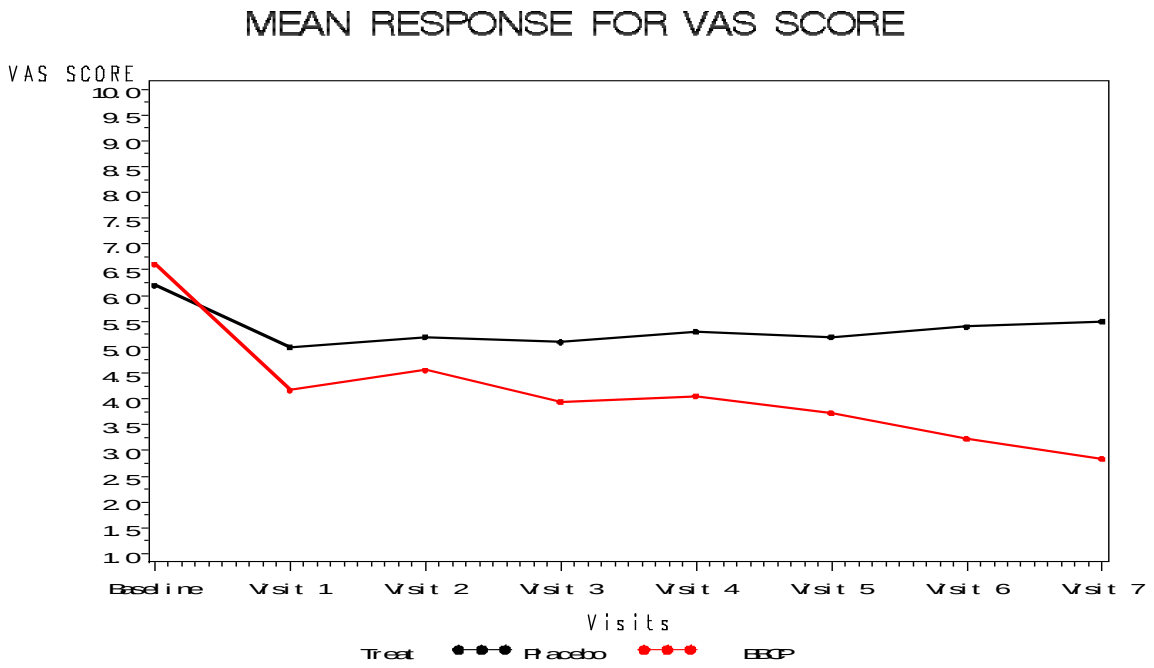
VAS Score Analysis

Box & Whisker Plot for VAS Score between Baseline & Visit 7

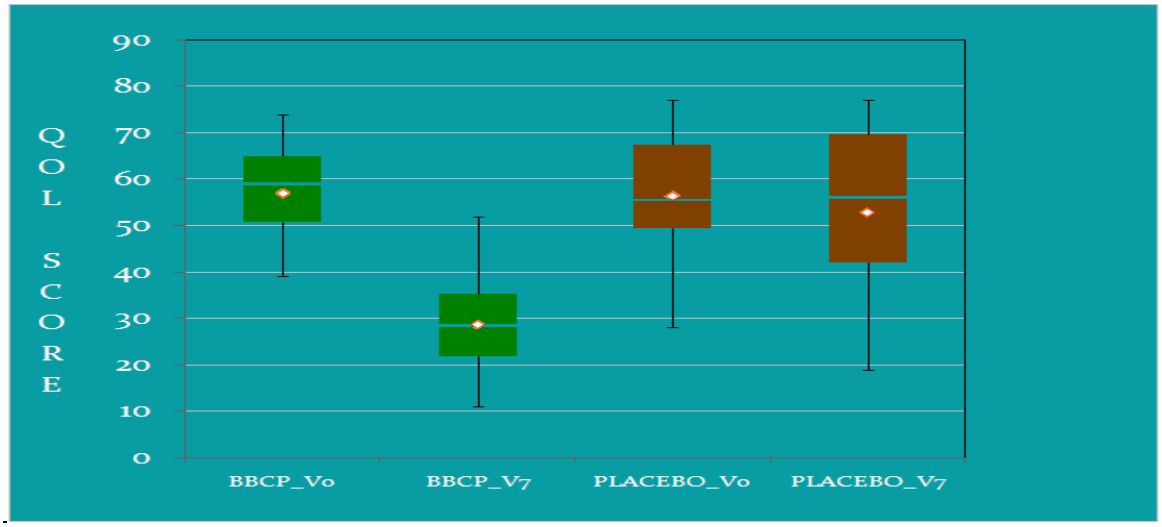


Out of 18 subjects receiving BBCP 14 (77.7%) subjects had shown good to better improvement in VAS score.

Statistically significant changes (p = 0.0001) were observed between groups BBCP and Placebo.

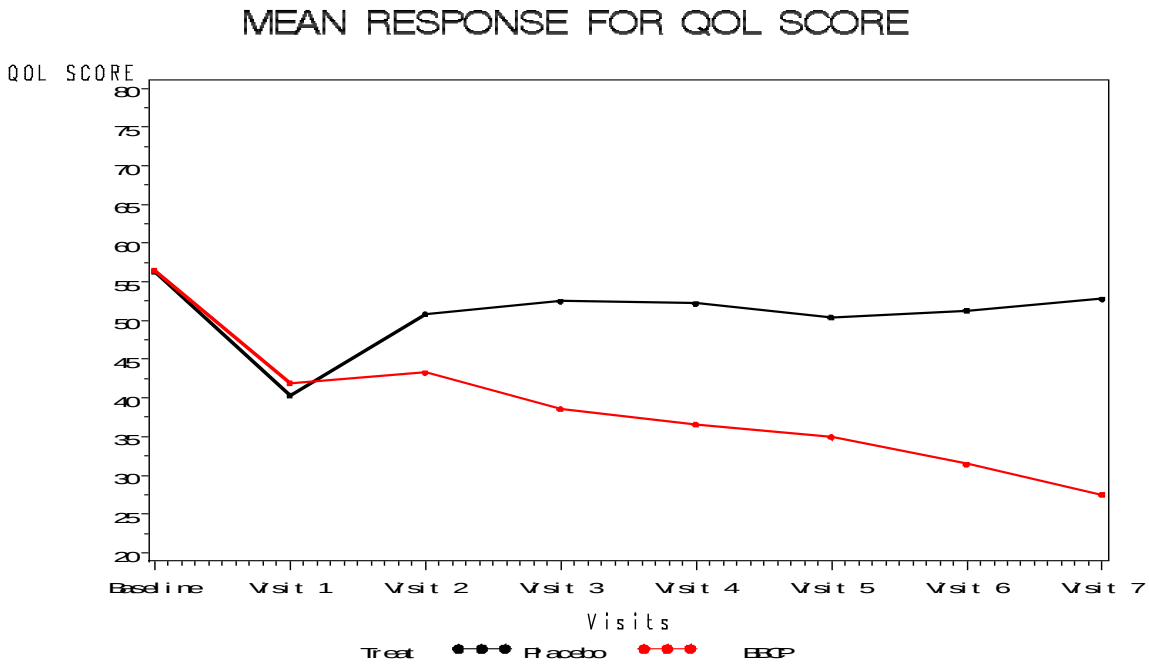


QoL Score Analysis



Out of 18 subjects receiving BBCP 16(88.8%) subjects had shown good to best improvement in QoL score

Statistically significant changes (p = 0.0001) were observed between groups BBCP and Placebo



Discussion

- The Primary objective of the study was to compare the efficacy and safety of Bovine Bone Collagen Peptide with that of Placebo for the management of Knee joint Osteoarthritis.

- Thirty subjects (30) with clinically diagnosed Knee joint Osteoarthritis were screened with all meeting study criteria. Two subjects (2) dropped out of the study, of them one citing the adverse event and one had lost to follow up.

- 28 enrolled subjects completed the study through the thirteen weeks treatment period and were evaluated in the statistical analysis as completers and the dropouts were considered for ITT analysis

- Out of 18 subjects receiving BBCP, 14 (77.7%) subjects had shown good to best improvement in WOMAC score **(p = 0.0001)** and 14(77.7%) subjects had shown good to better improvement in VAS score **(p = 0.0001)**.

- Of 10 subjects receiving Placebo none of the subjects had shown good to best improvements in WOMAC score and 01 (10.0%) subjects had shown good to better improvement in VAS score.

- The secondary end points was achieved through good to best improvement in QoL with 16 subjects (88.8%) **(p = 0.0001).**

- Four AEs were reported in BBCP group and were not related to the investigational product.

- All AEs were mild to moderate in nature and were resolved without any sequel.

- No case of death or SAE was observed.

- Analysis of vital signs and laboratory values did not reveal any significant adverse outcomes.

- A safe and effective nonsurgical therapeutic supplement like this would be a welcome addition to the therapeutic repertoire.

CONCLUSION

- Significant improvement in WOMAC score(F= 12.40, p=0.0001) and VAS Score (F=12.94,p<0.0001) between group from baseline to visit 7,from one to thirteen weeks in BBCP group, which in turn resulted in improvement of overall Quality of Life (F=15.35, p=0.0001).

- As the Investigational product is a nutritional supplement it has resulted in best improvements in subjects with grade 2 Osteoarthritis

- The present study demonstrated that oral ingestion of Bovine Bone Collagen Peptide is safe and can improve joint function and Quality of life in patients with knee joint Osteoarthritis.

A note on Dr V T Sriram, Auroville Healthcare

Dr.V.T.Sriraam is an MD in Pharmacology who currently holds the honorary position of Medical Director for Anna University where he sketched the curriculum design and renders wide range of courses in clinical research. A medical professional as well as a researcher, he is the founder, Managing Director and Medical Director of Auroville Healthcare, Chennai – a CRO which partners with various domestic and multinational pharmaceutical and biotechnology companies for their Phase II, III & IV trials.