



# Therapeutic Activity of Collagen and Rosehip Extracts: A Review

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

## **Article Information**

DOI: 10.9734/CJAST/2021/v40i3131549

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Complete Peer review History: <https://www.sdiarticle4.com/review-history/74137>

**Review Article**

**Received 14 August 2021**  
**Accepted 18 October 2021**  
**Published 01 November 2021**

## **ABSTRACT**

This article is an examination of the therapeutic activity of collagen and rosehip extracts. The scientific development and subsequent activity of collagen continues to influence the researchers all over the globe today. This article examines the research done and published by researchers and scientists. Consideration of current trends and data in scientific queries demonstrates further therapeutic aspects of collagen and rosehip extracts. Collagen hydrolysate is known to alleviate pain in knee joints and provide other protective effects in osteoarthritis, research papers and review articles from the past were considered as the basis of this work. Researchers have carried out experiments and statistically proven the role of collagen hydrolysate in joint disorders and different ortho related disorders. Collagen hydrolysate can provide symptomatic relief to the patients with osteoarthritis and according to the in vitro studies it can also be considered as a potential

candidate for its therapeutic properties. Clinical studies have indicated that collagen hydrolysate significantly reduces pain and disability. It also has various regenerating effects that can help restore the damaged cartilage. Component and chemo metric analysis of the rose hip was done and rosehip extracts were characterized to reveal their anti-oxidant and anti-inflammation properties using enhanced cross-linking mechanism and High-performance liquid chromatography. Collagen and rosehip extracts are clinically proven beneficial for osteoarthritis, rheumatoid arthritis, back pain, joint disorders, knee pain and post – ortho surgery conditions like pain and inflammation. A compilation of data is done in this article and explores options for therapeutic activity of hydrolysate for the treatment of osteoarthritis and other joint disorders and as a dietary supplement in athletes with activity-related joint pain. Anti-inflammatory and anti-oxidant properties of rosehip powder, identification and characterization of the active component GOPO and the assessment of rosehips based on the content of their biologically active compounds and rosehip extracts in ortho and ortho post-surgery

**Keywords:** Collagen; rosehip extracts; ortho; ortho post-surgery; review; therapeutic activity.

## 1. INTRODUCTION

Collagen is the major component of animal connective tissue that makes it an integral part of several body parts including tendons, ligaments, skin, and muscles. It functions as providing structure to the skin and strengthen the bones. It helps in maintaining the integrity of cartilage, which protects the joints because of its rubber like nature [1-6].

It's evident that as we age the bone mass deteriorates because of decrease in collagen level in the bones and other body parts which leads to development of degenerative disorders like osteoarthritis which is characterized by low bone density and linked to higher risks of bone fractures [7-10]. In recent years various studies have been conducted to show effective results of taking collagen supplements because of its ability to inhibit the bone breakdown and prevent conditions like osteoporosis, ortho arthritis etc [11-15]. Collagen supplements have become popular in the recent times as it reduces inflammation and stimulates collagen synthesis in the body. The supplements are hydrolyzed collagen which makes it easier for the body to absorb [16-19].

Researchers have theorized that intake of collagen supplements accumulates in the cartilage and stimulates the connective tissue to make collagen which results in lower inflammation and reduced pain in ortho related problems and ortho post surgeries as well [20,1]. In a recent study the effect of collagen hydrolysate was examined where 147 participants who took collagen supplements experienced reduced pain and inflammation in fitness related joint pains while the ones who

were just given a placebo did not show positive results.

Rosehip from *Rosa canina* fruits have been used as herbal remedies since ancient times. It is the round portion of the rose flower just below the petals, seed bearing part of the rose plant. Dried rose hip and its seeds have great medicinal value [22-24]. Rose hip is used for treatment of osteoarthritis and post ortho surgeries. Rosehip Extracts are effective in reducing joint pain inflammation and prevents damage as it contains polyphenols and anthocyanin. It also has antioxidant properties because of Vitamin C richness [25-30]. Antioxidants are substances that can override free radicals which are produced within the cells that damages the tissues and cause various diseases. Studies have found that Rosehip extracts can reduce the production of cartilage breaking enzymes.

A paper on Rosehip extracts, Marc Cohens explains how a standardized rosehip powder was developed to maximize the control of photochemical. This powder was used to demonstrate clinical benefits in conditions to osteoarthritis, rheumatoid arthritis and back pain. In conditions to osteoarthritis, rheumatoid arthritis, back pain and inflammatory bowel disease, there have been a number of clinical trials exploring the efficacy of rosehip powder preparation [31-38]. Hyben Vital. The first clinical trial was performed taking 100 patients who were radiographically proven with osteoarthritis of hip and knee. Among these patients, some of who were at the end stage or waiting for joint replacement were provided with either 2.5 g of standardized rosehip powder or placebo twice daily for 4 months [39,40]. Results revealed that 64.6% of patients who received rosehip, reported

with significantly reduced pain against placebo. Also, the patients who were treated with rosehip experienced improved hip flexion with no significant change observed for internal and external rotation of the hips or knee flexion.

## 2. METHODS

The study was conducted using four databases Google Scholars SAGE, DOAJ and PubMed. Selection of papers were done based on keywords and theme relevant to this review. Further the published papers from these databases were arranged in systematic order with respect to year of publication.

## 3. RESULTS AND DISCUSSION

### 3.1 Collagen of Cartilage and the Role of Collagen Hydrolysate in Joint Disorders

The current review article is based on the type of articular cartilage collagen and the role of collagen hydrocele late in the treatment of osteoarthritis and other joint disorders. Articular collagen are polymeric collagen found in mammals. Collagen hydrolysate it's known to alleviate pain in knee joints and provide other protective effects in osteoarthritis, research papers and review articles from the past were

considered as the basis of this work. A compilation of data is done in this article.

The use of collagen hydrolysate on the basis of its efficacy can help improve the clinical effects of the treatment in osteoarthritis and other arthritic conditions.

Collagen forms the maximum portion of articular cartilage. Collagen type 3 is found in normal as well as osteoarthritic human articular cartilage and it plays an important role in the wound healing process. In adult tissue, collagen type 2 synthesis can be accelerated up to 10 folds in a span of two weeks after the joint injury. Denaturation and proteolysis of matrix type 2 collagen is evident in normal and osteoarthritis joint surfaces which can be detected using specific antibodies. Articular chondrocytes express MMP 13 which plays an important role in cleaving type 2 collagen. MMP13 or collagenase 3 is responsible for the breakdown of cartilage collagen in osteoarthritis. Remodelling of collagen Type 1 base tissue can help in slowing the degradation process in osteoarthritis. Collagen hydrolysate is known to significantly increase the biosynthesis of type 2 collagen in chondrocytes. According to the preclinical studies less than 10% of collagen hydrolysate remains in the gastrointestinal tract indicating its

**Table 1. Therapeutic activity of collagen and Rosehip extracts in ortho**

Sr. No	Paper Title	Year
1	1)Collagen of articular cartilage 2)Collagen hydrolysate for the treatment of osteoarthritis and other joint disorders: a review of the literature	2001, 2006
2	24-Week study on the use of collagen hydrolysate as a dietary supplement in athletes with activity-related joint pain	2008
3	1)Laboratory and preclinical studies on the anti-inflammatory and anti-oxidant properties of rosehip powder – Identification and characterization of the active component GOPO 2)Assessment of rosehips based on the content of their biologically active compounds	2008 , 2017
4	A Novel Rose Hip Preparation with Enhanced Anti-Inflammatory and Chondroprotective Effects	2014
5	Comparing different preparations and doses of rosehip powder in patients with osteoarthritis of the knee: an exploratory randomized active-controlled trial	2014
6	Collagen supplementation as a complementary therapy for the prevention and treatment of osteoporosis and osteoarthritis: a systematic review	2016
7	The role of rose hip ( <i>Rosa canina L</i> ) powder in alleviating arthritis pain and inflammation – part II animal and human studies	2016
8	Assessment of Efficacy of Rosehip Extract in Treatment of patients with Osteoarthritis of Knee	2020
9	Role of Collagen Derivatives in Osteoarthritis and Cartilage Repair: A Systematic Scoping Review With Evidence Mapping	2020
10	Therapeutic Applications of Chondroitin Sulphate, Collagen and Rosehip Extract in the Musculoskeletal System	2020

absorption rate through oral administration. Pertaining to the efficacy of collagen hydrolysate it was observed that treatment of chondrocytes with 0.5 mg/mL collagen hydrolysate induced and increase in the collagen type 2 synthesis of the chondrocytes which was not observed in case of collagen free hydrolysate administration. According to the clinical studies collagen hydrolysate had improved the degenerative joint disease condition in patients with knee osteoarthritis. It significantly alleviated the pain. Oral administration of collagen hydrolysate treatment helps with improving the ability to climb stairs, soft tissue swelling, and knee effusion.

Collagen matrix of the articular cartilage plays an important role in controlling the mechanism of degradation in disease. Breakdown of collagen is a crucial part which accelerates the progression of osteoarthritis. Mutation and cartilage collagen can give rise to new gene products. This mechanism disturbs the framework of the cartilage matrix and can aggravate the clinical conditions in the patients. Hence molecular mechanisms should be devised keeping in consideration the functional integrity and the component of collagen in articular cartilage. Degeneration of articular cartilage in patients with osteoarthritis is due to the disorientation of the structural framework of the cartilage tissue. Therapeutic treatment using analgesic and anti-inflammatory agents can help with providing lubrication to the cartilage and improving the condition. Collagen hydrolysate can provide symptomatic relief to the patients with osteoarthritis and according to the in vitro studies it can also be considered as a potential candidate for its therapeutic properties. Clinical studies have indicated that collagen hydrolysate significantly reduces pain and disability. It also has various regenerating effects that can help restore the damaged cartilage.

### **3.2 Effect of Collagen Hydrolysate on Joint Pain in Athletes**

The study was carried out to determine the effects of collagen hydrolysate on the joint pain of athletes who experience joint pain despite being physically active and having no history of joint diseases. The study consisted of a population size of 147 people having a history of physical activity or currently involved in some kind of sports. The population was divided into 2 groups randomly. Group 1 consisted of 73 members who were put on a treatment of 10g collagen into 25 ml hydrolysate

administration and Group 2 consisted of 74 members put on a 25 ml of placebo medication consisting of xanthan. The study was carried out for a period of 24 weeks and 4 follow up visits at an interval of 6 weeks between each visit. The history of the subject was assessed with respect to prevalent conditions or any co-morbidities. Results were conferred with respect to the parameters consisting of pain, mobility, and inflammation. Five parameters that were considered for the comparison was the joint pain while walking, rest, standing, carrying objects and lifting. The outcomes indicated the higher efficacy of collagen hydrolysate as it had the higher negative values compared to that of placebo. In this study 147 people were considered for the study, out of them 97 people were evaluated for the evaluation. Group 1 consisted of people put on the collagen hydrolysate treatment. Group 2 consisted of people put on placebo treatment. There was no difference between vitamin and mineral supplement use in between Group 1 and Group 2. Joint discomfort was observed in 63 subjects i.e 29 treatment and 34 placebo. Both groups showed no difference in origin of discomfort like degenerative disease, sports injury, joint deformation, or genetic predisposition. No statistical difference was observed in the effects of the medication. The primary efficacy outcomes and the secondary efficacy outcomes were determined by the 24 week long study. The primary efficacy outcomes were based on the pain parameters and the secondary efficacy outcomes were based on the addition of alternate therapies. The primary efficacy outcomes indicated the higher efficacy of collagen hydrolysate compared to placebo treatment as the values of collagen hydrolysate were towards the higher negative values. Subgroup analysis with knee arthralgia had more pronounced results of collagen hydrolysate being effective.

Primary efficacy outcomes indicated that dietary supplementation of collagen on the athletes has good effects. Secondary efficacy outcomes indicated the alternative therapies have good effects in degenerative joint disease and joint discomfort or pain.

Collagen hydrolysate supplement helped alleviate the pain and need of analgesics for the treatment of osteoarthritis and increase mobility. Based on the prior studies it was observed that 78% of individuals experienced improvement in their joint movements. In this study the utility of

collagen hydrolysate was to be determined based on the 24 weeks long treatment and its potential as a supplement, for the same young individuals, involved in physical activity was considered for this study. For this a total of 147 individuals were incorporated out of which only 97 individuals can be accessed for the final results. They were divided into two groups Group 1 consisted of collagen hydrolysate treatment and Group 2 consisted of placebo treatment. The results were determined with respect to the arthralgia of the knee, joint pain and adverse effect of the medication. Initial stages of the study showed almost no difference, but at the end of 24 weeks, the difference between the treatment and the placebo was more profound. The study was divided into primary efficacy outcomes and secondary efficacy outcomes. Comparing the pain evaluation of treatment with the collagen hydrolysate versus placebo, the group with the collagen hydrolysate treatment reported lesser joint discomfort compared to the placebo. Alternative therapies showed higher efficacy of collagen treatment wherein after administration of 3 months, collagen hydrolysate as a supplement had good effects on joint discomfort in individuals who were physically active and did not have degenerative joint disease. Taken into consideration the preclinical studies and the alternate therapies it is observed that collagen hydrolysate has good potential for being used as supplementation which can be clearer by further researches and studies.

### 3.3 Antioxidant and Anti-Inflammatory Properties of Rosehip Powder and Characterization of the Bioactive Component

In the current study the component analysis of rosehip samples were done among 71 *Rosa* genotypes. Biologically active compounds were analyzed to determine their antioxidant properties. They were quantified and on the basis of the highest concentration of the biologically active compounds obtained the final results were concluded. In another part clinical studies were carried out to determine the effect of aqueous extract of Rosehip on the chemotaxis as well as chemiluminescence activity of human peripheral blood leukocytes *in vitro*.

For the characterization High performance liquid chromatography was performed on the methanol extracts. Roses with 71 different genotypes were collected and deseeded manually in a mortar and

pestle. DPPH radical scavenging activity was determined to check its antioxidant properties. Component and chemometric analysis of the rose hip was done. Characterization of active component GOPO with the help of aqueous solution of standardized Rose hip powder. Polymorphonuclear leukocytes were used to check its biological activity. Inhibition of the chemotaxis was determined with the help of control culture medium. Chemiluminescence was determined according to the oxidative burst response. Cell viability was checked with the help of trypan blue dye exclusion method under the microscope. GOPO was isolated with the help of sequential extraction and determined using HPLC.

Among the 71 rose genotypes ten of them consisted of the highest content of targeted biologically active compounds. Rosehip extract can be used for the development of osteoarthritis medication due to its inhibitory effect on chemiluminescence and inflammatory cytokines.

DPPH radical scavenging activity indicated the antioxidant activity value of the rose hip extracts. It was recorded in the form of ascorbic acid equivalent which ranges from 86.5 g/kg to 192.5 g/kg of ascorbic acid equivalent for dried Rose hips. The highest activity of carotenoids, tocopherol and flavonoids was observed. Among the carotenoids carotene and lycopene levels were determined from the various *Rosa* species. Tocopherol were determined with the help of HPLC- FLD. The polyphenolic compounds or the flavonoids screen using UHPLC - HRMS. Catechin, quercetin and Rutin peaks were observed. Among the Triterpenic acids, Urosolic, Oleanolic and betulinic acids were observed via the chromatographic separations and were known to have immunomodulatory activities. *Rosa dumalis* and *Rosa rubiginosa* species had the maximum quantity of biologically active compounds. Aquarius extract of Rose hip powder inherited the chemotaxis and chemiluminescence pain in the patients. It inhibited the respiratory burst of human polymorphonuclear size and executed an inhibitory effect on the inflammatory cytokines. GOPO battery effect on the chemotaxis and oxidative burst response which indicated the anti-inflammatory and antioxidant properties of rosehip. GOPO couple products can be used for the development of drugs for the treatment of osteoarthritis and other inflammatory diseases.

**Table 2. Collagen hydrolysate vs placebo (in joint pain)**

<b>Treatment</b>	<b>Walking</b>	<b>Standing</b>	<b>Rest</b>	<b>Carrying things</b>	<b>Lifting</b>
Collagen hydrolysate	-1.11 ± 1.98	-0.97 ± 1.92	-0.81 ± 1.77	-1.45 ± 2.11	-1.79 ± 2.11
Placebo	-0.46 ± 1.63	-0.43 ± 1.74	-0.39 ± 1.56	-0.83 ± 1.71	-1.26 ± 2.09

GOPO can be a potential candidate to develop new anti-inflammatory drugs for the treatment of rheumatoid arthritis and osteoarthritis as well as the treatment of certain inflammatory diseases. Rose powder does not interfere with the fibrinolysis or the coagulation cascade thus not affecting the platelets count. Hence it can be used for the treatment of patients with certain cardiovascular comorbidities too. It is a potentially safe alternative for the therapeutic administration in patients with osteoarthritis.

### 3.4 Anti-Inflammatory and Chondroprotective Activity of Rose Hip Powder

This research article is based on the anti-inflammatory and chondroprotective effect of Rosehip as it is known to attenuate arthritis.

**Methodology:** Comparative study was done between the 2 types of rosehip powder mixture. In the first type of mixture, rose hip was directly powder (A). In the second type of mixture the rose hip seeds were removed and then rose hips were powdered (B). The constituents of the powdered mixture were analyzed. Human peripheral blood leukocytes and primary chondrocytes were used for analysing the anti-inflammatory activity and chondroprotective effects. The cytokines chemokines and interleukins production was subjected to an analysis. The clinical efficacy of rosehip was determined according to the cytokines and chemokines like (IL-) 6, IL-12, CCL5, CXCL10. Statistical analysis was done to evaluate the results. Evaluation of the expression of matrix metalloproteinase to determine the inflammatory effects. According to the findings, seedless powdered form of rosehip showed higher efficacy compared to the seeded powder of rosehip.

**Conclusion/significance:** Difference in the composition of the two types of powders were determined. According to the constituents of the composition, the removal of seeds of the preparation showed higher level of  $\alpha$  tocopherol, with enhanced anti-inflammatory activities. Rosehip preparations had an effect on LPS/IFN- $\gamma$ -induced changes in the peripheral blood leukocytes at the transcriptional level. It also regulated the catabolic gene expression in the normal human chondrocytes.

Powder was obtained from rosehip fruits, wherein in one form the rosehip fruit was powdered along with the seeds (RH-A) and in the other form the fruit was powdered after the removal of the seeds (RH-B). Biological potency with respect to the composition of the two different powdered forms. RH-B had higher contents of ursolic acid, betulinic acid, 3-omega PUFAs showing an anti-inflammatory effect. RH-A had a higher content of GLGPG showing anti-inflammatory activity. Peripheral Blood Leukocytes (PBL) and primary chondrocytes (NHAC-kn) were checked for the anti-inflammatory and chondroprotective activity. Rosehip preparation had a significant effect on the secretion of chemokines. It reduced the levels of CCL5/RANTES, and CXCL10/IP10 and increased the secretion of CXCL8/IL-8 and CCL3/MIP-1 $\alpha$ . No effects were seen on the secretion of CCL11/eotaxin, CCL2/MCP-1, and CCL4/MIP-1 $\beta$ . RH preparation influenced the secretion of interleukins and cytokines. RH-B had higher efficacy compared to RH-A. However both RH-A and RH-B regulated the LPS/IFN- $\gamma$ -induced changes in PBL at transcriptional level. Administration of RHP decreased the IL-1 $\beta$  mRNA levels. Conversion of fatty acid into substrate for COX-1 in PBL proved that RHP regulated PGE2 in dormant PBL thus increasing it. These factors serve as the evidence that RH preparation has inflammatory effects. Chondrocytes with Osteoarthritis (OA) condition showed the presence of some upregulated catabolic genes. NHAC-kn with OA condition showed elevated expression of catabolic genes (MMP-1, MMP3, MMP-13, and ADAMTS-4), cytokine genes (IL-1 $\alpha$ , IL-6, and TNF- $\alpha$ ), and chemokines (CXCL8/IL-8, CCL5/RANTES, XCL2/MIP-2, and CXCL20/MIP-3 $\alpha$ ). Administration of RH-A decreased the expression of MMP-1 and MMP-3 by 50%, MMP-13 by 90%, ADAMTS-4 mRNA levels by 50%, CXCL8/IL-8, CCL5/RANTES, CXCL2/MIP-2, and CXCL20/MIP-3 $\alpha$  by 80%. RH-A was more potent than RH-B in altering the expression in the above chemokines, cytokines and interleukins. Principal component analysis (PCA) was done with respect to principal components (PCs) taken as meta-biomarkers. PCAs illustrations indicated that RH-A and RH-B had effects on PBLs based on the expression of 17 PBL proteins, 10 PBL genes, and 14 NHAC-kn genes. With respect to all the tests and illustration it was observed that the rosehip powder had a distinguishing effect on osteoarthritis with RH-B having greater impact on OA biomarkers compared to RH-A.

Biological activities of rosehip extracts were analysed on murine and human cellular models for its potential efficacy against osteoarthritis. RHP reduced production of nitric oxide, COX-2 dependent PGE2, various chemokines, and proinflammatory cytokines in LPS-activated murine macrophages, reduced the expression of interleukins, cytokines and chemokines CCL5/RANTES, CCL11/eotaxin, CXCL10/IP-10, CXCL2/MIP-2, and CCL20/MIP-3 $\alpha$  in chondrocytes and increased the production of GM-CSF and G-CSF in PBL. It improved the inflammatory response by decreasing cell mobilization in chronic OA conditions. Seedless powder of rosehip fruits (RH-B) enhanced the anti-inflammatory property of rose hip preparations due to the presence of higher contents of betulinic acid, ursolic acid, galactolipids, EPA, and DHA. Overall RH-B showed higher efficacy over RH-A on the anti-inflammatory and chondroprotective activity. Rosehip preparation had an enhanced in-vitro anti-inflammatory activity and chondroprotective activity on human peripheral blood leukocytes and primary chondrocytes.

### **3.5 Comparison of the Effects of Different Preparation of Rosehip Powder in Osteoarthritis of Knee**

In this study Rosehip powder was prepared in different dosage and composition and its efficacy was checked in patients with osteoarthritis of the knee. Rose hip powder was supplemented with vitamin C capsules. It was a 12 week randomised active controlled trial where in a total number of 150 patients with osteoarthritis were considered as the subjects for the study. The total number of subjects were divided into three numbers and the treatment was administered into 3 different parts within each group of members. The outcome was recorded in the form of the treatment administered to the patients. Comparative study was done within treatment A treatment B and treatment C. Here the rosehip powder preparation was prepared in different proportions and forms. The preparation of rosehip powder was comparative between the original powder and the enhanced powder. The enhanced rose powder showed almost similar efficacy compared to the original one.

Random population having osteoarthritis consisting of 150 people were divided into three groups and administered the treatment. Treatment A consisted of original Rose hip powder (4500 mg) with seeds and vitamin C (80 mg) 6 capsules/day. Treatment B consisted of

enhanced Rose hip powder (4500 mg) with new seedless rosehip powder and vitamin C (80 mg) 6 capsules/day. Treatment C consisted of enhanced Rose hip powder (2250 mg) with new seedless rosehip powder and vitamin C (80 mg) 3 capsules/day. The study was 12 weeks long and the outcome measures were assessed every four weeks. The statistical analysis, clinical outcomes, adverse events and ancillary analysis of the results were done. The groups were prepared based on the similar clinical characteristics. Among the groups no significant difference was observed with respect to the pain on walking. All the three rose hip preparations showed equivalent efficacy. However the quality of life and the KOOS symptoms were improved in the groups with enhanced Rosehip power administration. Minimal adverse events were reported in all the groups with some side effects being evident in group B and C over group A however it was not statistically significant. Mild side effects involved abdominal and intestinal symptoms and nausea. Considering the ancillary analysis the overall outcome of the trial indicated that the difference was very small and indicated that all the three treatments were equally effective.

The outcome of the report suggested that different preparation and dosage of rose powder in patients with osteoarthritis of knee were evident in reducing pain while walking. The use of enhanced Rose hip powder can be of benefit as the quantity required to achieve similar effect is nearly half of what is required with the original powder. The analgesic properties of the Rosie powder due to the presence of active substances like flavonoid, carotene, galactolipids and Vitamin C contributed towards the higher efficacy of the treatment. However the clinical relevance of the study is yet to be reported due to the absence of a placebo or a control group. KOO's symptoms were improved in the presence of enhanced Rosehip powder preparation. As the overall outcome the pain during walking was decreased and changes were observed in the knee injury along with osteoarthritis outcomes were enhanced indicating advantage of the enhanced rosehip powder preparation. Enhanced rosehip powder preparation proved to be equally effective as that of the original product within the quantity of half of what was used as the original product.

### **3.6 Collagen Supplement as Complementary Therapy**

Osteoarthritis is a degenerative joint disease of which the drug development is being extensively



researched upon. To facilitate the same in the current review the collagen supplement as a complementary therapy for the treatment of osteoarthritis is being studied. Scientific articles based on the action and role of collagen hydrolysate on cartilage and bone and its effects on osteoarthritis. Collagen hydrolysate has various articular cartilage protective properties and also provides symptomatic pain relief. It can help in increasing the absorption of amino acids in plasma as well as promote bone regeneration. The article is a compilation of the various research done in vitro and in Vivo on human cells and animal models. 9 experimental articles out of which 5 were based on human models and three were based on animal models and 1 in vitro study was carried out. The outcomes of an experiment consisting of humans in which whey protein was tested against the efficacy of collagen hydrolysate indicated that collagen hydrolysate helped in maintaining the weight and promoted low excretion of nitrogen. It helps in maintaining the weight and muscle mass. In another in vivo experiment in mice, collagen hydrolysate prompted higher growth and differentiation of osteoblast and osteoclast which rendered osteo protective activity. In another control group collagen hydrolysate helps in bone mineralization and conserve the composition and strength of the bone. In a study carried out on human athletes it was observed that collagen hydrolysate helped in the improvement of knee arthralgia which led to the reduction of pain and protection of cartilage. It also helped in polish federation and cellular growth of cartilage. Different doses of administration of collagen hydrolysate help in increasing the amino acid absorption and haptoglobin in plasma. In a study where collagen hydrolysate was tested against the placebo gel capsule, it showed that collagen hydrolysate had higher efficacy and was safe to use as a supplement. Aging continues to be an important factor which brings along a lot of chronic disease and osteoarthritis this being one of the the most prevalent one. In order to improve the current medication and treatment of arthritis it's important to devise medication and treatment that must be more effective. Being asymptomatic in nature, osteoarthritis often goes undiagnosed at its earliest stage. Osteoarthritis is characterized by its gradual destructive nature wherein it affects the joints and the osteophyte formation. It is a degenerative joint disease which affects the elderly and can cause chronic discomfort and pain. Collagen being a molecule composed of three amino acids can help in biosynthesis and regeneration. According to the

prior studies and research it was found that collagen hydrolysate has an ability to accumulate in cartilage and bone. Type 1 collagen being the most abundant in connective tissue along with partially hydrolyzed collagen and collagen hydrolysate can greatly contribute to the stability and regeneration of cartilage. Combining collagen hydrolysate in an essential amino acid deficient diet can help in restoring the nitrogen levels in the body. In the menopausal state due to the loss of bone integrity due to hormonal changes can be potentially restored with the administration of collagen as observed in various in vivo studies. Prolonged use of chemicals and drugs can lead to toxicity and accumulation in the tissues but collagen being predisposed in the cartilage helps in keeping the toxicity to the minimum level thus proving an efficient choice as a therapy and osteoarthritis. Hence collagen hydrolysate has great potential in therapeutic administration for the treatment of osteoporosis and osteoarthritis due to its protective effect on articular cartilage and also due to its pain relieving properties. Moreover for the studies and research is needed to develop an effective supplementation with higher therapeutic efficacy.

### **3.7 Role of Rosehip Powder in Arthritis Pain and Inflammation**

In this research article the extracts of Rose hip *Rosa canina* are used to determine its efficacy and herbal properties. Animal studies were done with the help of Rosa preparation and were tested against the Placebo. Anti-inflammatory and antinociceptive screening was done in the mice. The metabolism rate with respect to obesity was checked with the help of dose-dependent administration of rosehip. Animal studies were carried out on rats, horses and dogs. Human studies were done to evaluate the effect of Rose abstracts on osteoarthritis. It was checked for its improvement on knee injury and osteoarthritis outcome score. Double blinded clinical studies with placebo controlled group work carried out on osteoarthritic and rheumatoid arthritis patients. Substantial evidence to support the anti-inflammatory activity of rosehip extract was obtained. It also had some antinociceptive activity. Prolonged administration of rosehip extract does not resort to any side effects for gastrointestinal bleeding. Rose hip extract showed anti-inflammatory and pain relieving properties in mice. It inhibited the inflammatory swellings of the foot pad. 8 significantly inhibited the increase in vascular permeability thus controlling the inflammatory condition. In male

Swiss albino mice Rosemary extract was successful in reducing the number of abdominal contractions which contributed to the pain relief. Rosehip extract has potential anti-ulcerogenic effects. They have Cox 2 inhibitor effects thus do not cause gastrointestinal bleeding. The anti-inflammatory and pain relieving properties are due to the synergistic interaction of the bioactive compounds in the rose hip extracts. The fatty acids present in the extract that is linolenic and Alpha linolenic acid inhibited the Cox 2 enzyme. On a study carried out in mice it was observed that rosehip extract promotes the expression of PPAR- $\alpha$  mRNA, hence increasing the lipid metabolism. Significant changes were also observed in the mouse paw swelling and along with that it also provided ulcerogenic protection. In a placebo controlled study of rosehip powder in horses it was observed that the chemotaxis of neutrophils significantly reduced in rose powder therapy and significant improvement was observed in the vitamin C levels in horse's plasma. The overall effect was reported with respect to the speed and fur quality of the animals. Studies have suggested rose powder as a promising agent rendering anti inflammation and pain reducing properties. This is attributable to the bioavailability of the active compounds present in the extract. It helps in improving the knee joint function which is beneficial in the treatment of osteoarthritis patients. A decline in blood levels of inflammatory markers was reported in the clinical studies carried out using rosehip extracts. In vitro studies focused on the anti-inflammatory properties of rose powder observed in its various combination and preparation.

### 3.8 Efficacy of Rosehip Extract in Osteoarthritis of Knee

In this research paper the efficacy of Rosehip Extract was assessed against the effects of Osteoarthritis of Knee. This study was carried out on patients admitted for osteoarthritis in, they were screened for the presence of Osteoarthritis. Patients screened with osteoarthritis were randomly divided into two groups and they were taken as the sample population. In one group the rosehip extracts were administered (Group 1) and the other group was put on placebo orally. The study was conducted for a span of 3 months. Treatment was administered to both the groups and they were examined at an interval of every 4 weeks for efficacy parameters and safety parameters. Efficacy parameters were to scrutinize the pain, stiffness and physical

functioning. Safety parameters were to determine if the drug had any adverse reaction.

Group 1 who were administered Rosehip extracts showed better overall improvement compared to Group 2 who were administered Placebo medication. The efficacy parameters with respect to the pain, stiffness and physical functioning, rosehip extracts showed an enhanced effect. The safety parameters were in favor of both the types of treatments and did not pose any potential threat on the patients. The overall efficacy of rosehip extractions on patients with osteoarthritis yielded good results thus giving an upper hand to indulgence of rosehip extraction as a possible treatment for patients with osteoarthritis of knees. A total of 75 patients diagnosed with osteoarthritis were considered for this study. The clinical history, physical examination and other assessment was done prior to this study. In this study the treatment was an add on therapy coupled with the regular treatment that was administered to the patients. The patient population was homogeneous with consideration of similar age groups. In Group 1 a total of 35 patients with osteoarthritis were given 1.5g of rosehip extracts twice a day, orally for a span of 3 months as an add on therapy. In Group 2 a total of 40 patients were given placebo twice a day orally for 3 months as an add on therapy. They were examined at regular intervals of 4 weeks at 4, 8 and 12 weeks to check the efficacy and safety parameters. According to the WOMAC Scores Group 1 showed enhanced improvement compared to Group 2 in joint pain. At an interval of 4, 8 and 12 weeks rosehip preparation showed better effects on joint pain, with the maximum mean difference at 12 weeks' time. WOMAC scores revealed Group 1 had increased improvement in stiffness compared to Group 2, with the maximal effect at the 12 weeks. WOMAC scores at 4, 8 and 12 weeks for the physical function also showed improved efficacy of Group 1 compared to Group 2. Adverse Drug Effect of was observed to be minimal in both groups with mild to moderate symptoms of Gastritis, Vomiting, Diarrhea, Nausea.

Study was carried out in a group of 75 patients diagnosed with osteoarthritis. The study was an add on therapy administered along with the standard treatment. The population was randomly divided into 2 groups, wherein in the Group 1 there were 35 individuals who were administered rosehip extraction and in Group 2 there were 40 individuals who were administered

placebo medication. According to the study the maximum number of patients belong to the age group of 40-59 and more females were affected than male with a male to female ratio of 1:2.5 indicating the maximal progression of osteoarthritis at a particular age as a result of degradation of the articular cartilage due to cytokines such as adiponectin, leptin and resistin triggering the inflammatory response favouring being observed more in female compared to males. Osteoarthritis can be more prevalent in females compared to males due to hormonal changes during menopausal phase and demographically within females from urban population than rural population due to sedentary lifestyles. WOMAC scores indicated rosehip extracts had better efficacy as a complementary treatment over the placebo treatment. This study suggests rosehip extract coupled with paracetamol provides higher efficacy with negligible side effects and interference with other metabolic processes. Thus as a result the entire study provides substantial proof to favour the market preparation of rosehip extracts as a complementary treatment.

### **3.9 Significance of Collagen Derivatives in Osteoarthritis**

This is a review article consisting of the compilation of 16 pre-clinical and 25 clinical studies. It focuses on the importance of collagen and its derivatives in osteoarthritis and cartilage repair. The review is based on the data present in the papers published in preclinical and clinical studies. The papers were selected from different databases. The geographical location of the studies were taken into consideration. Various graphical and statistical methods were incorporated. The objective of this review was to collect substantial data to enhance drug development in the treatment of osteoarthritis. The collagen derivatives in concern were collagen hydrolysate and undenatured collagen. Oral administrations were incorporated for the study. The overall results of collagen derivatives and its effect on osteoarthritis. Study was based on the in-vitro and in-vivo studies. According to the geographical distribution of the study, the individuals largely belonged to Asia and very few to the USA. From Asia the clinical subjects belonged to China, Japan and some from India. Pre-clinical studies were conducted in-vitro. Effects of collagen hydrolysate were determined with respect to the cartilage metabolism, degradation and inflammatory mediator's levels. They were ineffective or

detrimental to articular cartilage in pathological condition. Along with that, undenatured collagen was also checked for its efficacy, with the conclusion that it had protective effect on articular cartilage. Clinical studies with undenatured type I collagen and undenatured type II collagen within the duration of 3-6 months and one 11 months long conducted in comparison with placebo indicated the beneficial effects of collagen in Osteoarthritis patients. This is a review on preclinical and clinical studies on the effect of collagen and its derivatives on Osteoarthritis. Most of the studies were conducted in Asia and America. The conducted studies favored the usage of collagen supplements in osteoarthritis treatment. In-vivo studies of collagen derived from dietary sources indicated its role in decreasing cartilage destruction and enhancing cartilage repair. Collagen extracts from various sources and different molecular weights were used in the studies. The preclinical studies had added on the beneficial effects of collagen in veterinary medicine too. Apart from that collagen supplements have also shown efficacy in improvement of joint comfort. It was also observed that bovine chondrocytes with degraded collagen promoted hyaline cartilage formation and prevented fibrous tissue formation. Thus collagen derivatives in the form of dietary supplements may be an important tool in the therapeutic treatment of Osteoarthritis. Apart from that, collagen derivatives also showed minimum to no toxicity in the studies conducted in in-vitro or in-vivo models. In the final analysis considering all the types of treatment and studies with collagen derivatives against placebo focused on the good scope of collagen and its derivatives on its efficacy in osteoarthritis and also keeps the door open to more research and development in this area for the production and administration in therapeutic treatment of osteoarthritis

### **3.10 Application of Collagen and Rosehip Extracts in Musculoskeletal System**

The review article is based on the collected data on the role of and application of collagen and rosehip extracts in the musculoskeletal system diseases between the years 2000 and 2020. Collected data is from the prior Studies and Research activities on the application of collagen and rosehip extract. Papers were selected from various databases. This is based on the compilation of the observations of the clinical

studies. In-vitro studies favored the use of collagen and rosehip extracts for the therapeutic treatment due to its antioxidant and other preventive properties. Collagen is a structural protein present in the connective tissues in the body and in the muscles, bones, tendons and skin muscle found in three types. Loss of Type 1 collagen can result in musculoskeletal system degeneration. Collagen has a lot of significance in Physio pathological conditions related to Amyloidosis. Lack of collagen can lead to rapid degeneration of joints in osteoarthritis. Supplementation of Vitamin C along with collagen can help accelerate the Type 1 collagen synthesis by reducing the oxidative stress parameters. The rate of collagen synthesis was lower in women taking oral contraceptives. Muscle collagen was found to be lower in postmenopausal women undergoing estrogen displacement therapy. The study on patients undergoing maxillary anterior implant those who were administered collagen showed significant changes which were observed in the vertical dimension of the Buccal soft tissue as well as in the mean Bucco-Lingual tissue. Rose extracts were obtained from the plant *Rosa canina* and it was assessed for its efficacy in the treatment of osteoarthritis respective to the pain. The results indicated a significant improvement in the joint mobility as well as reduction of pain and overall symptoms of osteoarthritis in patients undergoing the rosehip extract therapy compared to the placebo treated patients. Antioxidant effects of Rose hip extract was determined according to its phytochemical composition. It has shown to reduce the symptoms of rheumatoid

inflammation. Ascorbic acid played a vital role in helping reverse the damage caused by ROS production. Rose hip extract helped in the inhibition of osteoarthritis by neutralization of RONS. It also has anti-inflammatory action as well as antidiabetic and anticancer effects. Routine consumption of Rose hip powder improved the knee joint function and health in the knee related walking restrictions.

The overall outcome of the results focus on the findings that rosehip extracts and collagen have good effects in the in vitro cell studies. Apart from that they also have various preventive properties such as antioxidants and anti-inflammatory. They also help with the knee joint pain reduction as well as regeneration of bone tissue. However more clinical studies need to be done in order to effectively incorporate the therapeutic administration of these compounds in the treatment.

### 3.11 Degradation and Regulation of Type II Collagen in Articular Cartilage in Osteoarthritis

Years of report says that the pathogenicity of osteoarthritis, rheumatoid arthritis as well as other inflammatory arthritis have shown an underlying problem due to the degeneration of articular cartilage which leads to loss of joint function. This study involved the investigation of structure and function of articular cartilage (i.e. chondrocyte and collagen fibrils) that form the endoskeletal backbone of the extensive

**Table 3. Therapeutic activity of collagen and rosehip extracts in ortho**

Sr.No.	Paper Title	Year
1	Type II collagen degradation and its regulation in articular cartilage in osteoarthritis	2002
2	The clinical effectiveness of rosehip powder in patients with osteoarthritis. A systematic review	2007
3	24-Week study on the use of collagen hydrolysate as a dietary supplement in athletes with activity-related joint pain	2008
4	Collagen Scaffolds for Orthopedic Regenerative Medicine	2011
5	Rosehip-An evidence based herbal medicine for inflammation and arthritis	2012
6	A novel rose hip preparation with enhanced anti-inflammatory and chondroprotective effects	2014
7	Collagen supplementation as a complementary therapy for the prevention and treatment of osteoporosis and osteoarthritis: a systematic review	2015
8	The role of rose hip ( <i>Rosa canina L</i> ) powder in alleviating arthritis pain and inflammation – part II animal and human studies	2016
9	Evaluation of the effect of oral administration of collagen peptides on an experimental rat osteoarthritis model	2017
10	Long-Term Effectiveness of Polymerized-Type I Collagen Intra-Articular Injections in Patients with Symptomatic Knee Osteoarthritis: Clinical and Radiographic Evaluation in a Cohort Study	2020

extracellular matrix which further helped in detection of joint degeneration and its progression in OA. This overview and other laboratories have captured some of the recent developments in understanding and because the normal content of aggrecan in cartilage ordinarily excludes gadolinium from the extracellular matrix. This technology offered much promise in the detection of early disease and in studying its progression". Recent studies involved combinations of degradation and synthesis markers and derivative markers (collagenase cleavage epitope assays) have shown that it is now possible to predict clinical outcome from the JSN over a period of 1–2 years. These new developments offer much promise for the future management of clinical trials whereby drug treatment for one to two months may lead to a change in synthesis or degradation.

### **3.12 A Systematic Review- The Clinical Effectiveness of Rosehip Powder in Patients with Osteoarthritis**

A standardized rosehip powder was developed to maximize the control of photochemical. This powder was used to demonstrate clinical benefits in conditions to osteoarthritis, rheumatoid arthritis and back pain. A meta-analysis of the three randomized controlled trials of osteoarthritis patients was performed which included 287 patients with a median treatment for a period of 3 months. This reported that patients who were treated with rosehip powder responded more aggressively as compared to placebo with a high frequency of relieved pain.

The clinical experiment based on the traditionally herbal medication of rosehip powder suggests that standardized rosehip powder may offer an effective first line therapy and is a viable replacement for conventional drug therapies such as NSAIDs in osteoarthritis.

In Randomized Controlled Trials, the first clinical trial was performed taking 100 patients who were radiographically proven with osteoarthritis of hip and knee. Among these patients, some of who were at the end stage or waiting for joint replacement were provided with either 2.5 g of standardized rosehip powder or placebo twice daily for 4 months. Results revealed that 64.6% of patients who received rosehip, reported with significantly reduce against place The main analysis was based on the experiment observed from the efficacy of standardized rosehip powder.

management of the pathobiology of OA such that new therapeutic targets might get identified. "The use of magnetic resonance imaging in conjunction with the contrast medium gadolinium permits early detection of a loss of aggrecan In addition, rosehip may also offer benefits in other conditions such as back pain and rheumatoid arthritis. In another clinical trial, after 1 year surveillance of 152 patients, scientists found that rosehip provided significant pain relief for patients with acute exacerbations of chronic back pain.

### **3.13 The Use of Collagen Hydrolysate as a Dietary Supplement in Athletes**

Collagen hydrolysate is a nutritional supplement that has been shown to exert an anabolic effect on cartilage tissue. Its administration appears beneficial in patients with osteoarthritis. A prospective, randomized, and placebo-controlled, double-blind study was conducted at Penn State University in University Park, Pennsylvania. During the study phases in relation to the parameters referring to pain, mobility, and inflammation; it was observed that the primary efficacy parameter was the change in the visual analogue scales from baseline.

When data from all 97 subjects were evaluated, it was found out that 6 parameters showed statistically significant changes with the dietary supplement collagen hydrolysate (CH) compared with placebo: joint pain at rest, assessed by the physician (CH vs. placebo (-1.37 +/- 1.78 vs. -0.90 +/- 1.74 (p = 0.025)) and five parameters assessed by study participants: joint pain when walking (-1.11 +/- 1.98 vs. -0.46 +/- 1.63, p = 0.007), joint pain when standing (-0.97 +/- 1.92 vs. -0.43 +/- 1.74, p = 0.011), joint pain at rest (-0.81 +/- 1.77 vs. -0.39 +/- 1.56, p = 0.039), joint pain when carrying objects (-1.45 +/- 2.11 vs. -0.83 +/- 1.71, p = 0.014) and joint pain when lifting (-1.79 +/- 2.11 vs. -1.26 +/- 2.09, p = 0.018). This was the first clinical trial of 24-weeks duration to show improvement of joint pain in athletes who were treated with the dietary supplement collagen hydrolysate. The results of this study have implications for the use of collagen hydrolysate to support joint health and possibly reduce the risk of joint deterioration in a high-risk group. Despite the study's size and limitations, the results suggest that athletes consuming collagen hydrolysate can reduce parameters (such as pain) that have a negative impact on athletic performance.

### **3.14 Collagen Scaffolds- A Biomaterial for Orthopedic Regenerative Medicine**

Collagen and collagen-based scaffolds provide distinct advantages as biomaterials for use of regenerative medicine applications. Since collagen scaffolds have been widely used due to its biocompatibility and biodegradability properties, these scaffolds essentially provide a template for new tissue formation and are either seeded with cells prior to implantation or are implanted directly into the injured site and the body's own cells populate the construct to facilitate healing. This review focuses on the use of collagen and collagen-based scaffolds for tissue engineering applications in orthopedics. Relatively poor mechanical properties are often perceived to limit their usefulness for orthopedic applications. These problems can be overcome through enhanced crosslinking mechanisms or through the addition of a second, stiffer phase such as hydroxyapatite, thus allowing tailored composite scaffolds to meet specific tissue requirements. This overview highlighted the current state of the art of these scaffolds and considers the exciting prospects and future directions of collagen-based technologies for orthopedic regenerative medicine. The major concern in the field of tissue engineering is that the core degradation evolved from the lack of nutrient delivery and waste removal from the center of tissue engineered constructs and arises from an inadequate blood supply throughout the implanted tissue. An alternative approach is, using a cell-based approach, to engineer micro vessels (capillaries) into the construct prior to implantation, and it is envisaged that the presence of these nascent vessels might prevent the occurrence of avascular necrosis in vivo. A recent work from a laboratory took place, where they used co-cultures of MSCs and endothelial cells seeded on collagen-GAG scaffolds in vitro and demonstrated the formation of a vascular network inside the scaffold within two weeks in culture.

### **3.15 Reveal of Rosehip Extract as an Herbal Medicine for Arthritis**

A standardized rosehip powder was developed to maximize the control of photochemical. This powder was used to demonstrate clinical benefits in conditions to osteoarthritis, rheumatoid arthritis and back pain. An observation took place where it was proved that standardized rosehip powder

can be a replacement for conventional therapies used in arthritis. A meta-analysis of the three randomized controlled trials of osteoarthritis patients was performed which included 287 patients with a median treatment for a period of 3 months. The clinical experiment based on the traditionally herbal medication of rosehip powder suggests that standardized rosehip powder may offer an effective first line therapy and is a viable replacement for conventional drug therapies such as NSAIDs in osteoarthritis. In conditions to osteoarthritis, rheumatoid arthritis, back pain and inflammatory bowel disease, there have been a number of clinical trials exploring the efficacy of rosehip powder preparation. It should be noted that all clinical research on rosehip has been performed on the standardized, patented extract with the trials being supported by the manufacturer, Hyben Vital. The first clinical trial was performed taking 100 patients who were radiographically proven with osteoarthritis of hip and knee. Among these patients, some of who were at the end stage or waiting for joint replacement were provided with either 2.5 g of standardized rosehip powder or placebo twice daily for 4 months. Results revealed that 64.6% of patients who received rosehip, reported with significantly reduced pain against placebo. Also, the patients who were treated with rosehip experienced improved hip flexion with no significant change observed for internal and external rotation of the hips or knee flexion.

### **3.16 A Standardized Rose Hip Preparation- Its Enhanced Anti-Inflammatory and Chondroprotective Effects**

Rose hip powder (RHP) alleviates osteoarthritis (OA) due to its anti-inflammatory and cartilage-protective properties. Substances contained in RHP might contribute to its clinical efficacy. This review is based on the preparation of rosehip powder and its effects on inflammatory diseases especially in Osteoarthritis. Rosehip powder was prepared from *Rosa canina*. RH-A consists of dried rose hip powder and RH-B was prepared from dried rose hip, where the seeds had been removed before the preparation of the powder. In this study, a new form of rosehip powder has enhanced in vitro anti-inflammatory and chondroprotective properties in human peripheral blood leukocytes and primary chondrocytes. The distinct biological activity of RH-A and RH-B

correlated with different contents of constituents: RH-B contained higher amounts of ursolic acid, betulinic acid, GLGPG, and DHA. Of those, ursolic acid and betulinic acid and 3-omega PUFAs, but not  $\beta$ -carotene, vitamin C, or vitamin E, displayed anti-inflammatory effects (data from Article ID 105710). Removal of seeds increased the contents of  $\alpha$ -tocopherol Mediators of Inflammation 3 and GLGPG; the latter had anti-inflammatory properties. Other constituents (e.g., vitamin C) were homogeneously distributed in rose hip fruit parts. In this study, a panel of biological activities of rose hip powder prepared from the whole fruit or from shells has been compared. It provides evidence that cellular features related to inflammatory responses and cartilage destruction were modulated by the complex mixture of substances contained in RHP.

### 3.17 Collagen Supplementation- A Remedy Used For the Prevention and Treatment of Osteoporosis and Osteoarthritis

Collagen hydrolysate is known as a safe nutraceutical, whose combination of amino acids stimulates the synthesis of collagen in the extracellular matrix of cartilage and other tissues. This study was made to review the current status of collagen hydrolysate in the treatment of osteoarthritis and osteoporosis. The observation involved 9 experimental articles with in vivo and in vitro human models, which found out that the use of different doses of collagen hydrolysate were associated with the maintenance of bone composition, strength, proliferation and the cell growth of cartilage. Collagen hydrolysate is of interest as a therapeutic agent of potential utility in the treatment of osteoarthritis and osteoporosis. Its high level of safety makes it attractive as an agent for long-term use in these chronic disorders.

Nine experimental articles were identified as the basis for discussion in this review. The nine included: five research articles with human models, three with animal models, and one that evaluated, respectively, in vitro models (human cells) and animal models. OA is a degenerative joint disease characterized mainly by a slow and gradual destruction of cartilage with a narrowing of joint space, osteophyte formation and bone sclerosis synovitis<sup>12, 13</sup> and its exact cause is still unknown. It usually affects middle-aged adults and although it is one of the main causes of chronic disability, conventional therapeutic

treatments are still limited, as their results are minimal, and prolonged use of these drugs can cause toxicity. As a result, the dietary supplement industries are increasingly investing in the development of supplements in order to delay the disease by directly supplying natural compounds, in order to inhibit or enhance the role of biological mediators to preserve the structural integrity of the joint. Collagen hydrolysate has a positive therapeutic role in osteoporosis and osteoarthritis: potentially increasing bone mineral density, having a protective effect on articular cartilage and, primarily, providing symptomatic relief of pain.

### 3.18 The Role of Rosehip Powder in Reducing Arthritis Pain

Rosehip from *Rosa canina* fruits have been used as herbal remedies since ancient times. This review explains about the component compounds which might exert the effect of ingredients present in rosehip. Factors which affect the quality and quantity of active ingredients in the rose hip products include the subspecies of the particular *R. canina* from which the fruits are harvested, the environment during plant growth, time of harvesting, and the amount of seeds and shells/husks incorporated into the preparation. Studies that have been performed during the last 2 decades indicate that the treatment of patients with different types of joint disease with rose hip powder based on a subspecies of *R. canina* containing a certain galactolipid (GOPO) can alleviate pain, improve daily activity, and even reduce the consumption of regular pain relievers. Although the number of publications of randomized and placebo-controlled clinic studies with rosehip is small and the overriding evidence is that the anti-inflammatory effects from administration of rose hip preparations containing both shells and seeds are superior to preparations containing shells alone. Clinical Study- The rose hip preparation used was again based on the natural amount of seeds and shells from a subspecies of *R. canina* (Lito). The fruits were dried by using a special patented drying procedure, which necessitates that the plants be held at temperatures never exceeding 40°C. In this study the results of testing a rose hip preparation on humans was reported as follows: 13 healthy volunteers were each treated with 45 g of rose hip powder daily for a period of 4 weeks, which was followed by at least 1 month of withdrawal and further treatment with 10 g rose hip powder daily for a final 4-week period. There was a

significant decline in CRP as the result of 4-week treatment with the high dose of rose hip powder.

In the Winther et al study, 11 the patients with osteoarthritis were administered 5 g daily dosage of either rose hip powder or placebo and the body weight of the study subjects were in the range from 50 to 122 kg. Consequently, the lower the body weight, the higher the dose of rose hip or placebo per kg. In principle, the lightest patients got approximately double the dose per kg body weight received by the heaviest study participant. When a correlation of weight against symptom score on pain was made for the active treatment and placebo groups, there was a significant negative correlation between body weight and the reduction in pain scores only in the group treated with rose hip (correlation coefficient -0.41, P-value =0.014) after 3 months of treatment. The same observation was made in the rose hip study on patients with RA who were treated daily with 5 g of either rose hip or placebo for 6 months.

### **3.19 The Effect of Oral Medication of Collagen Peptides- An Investigation Using Experimental Rat Osteoarthritis Model**

Collagen peptides (CP) are produced by the hydrolysis of gelatin (heat-denatured collagen) by proteases and are utilized as a component of nutraceuticals. The current study investigated the effect of CP on the articular cartilage of OA by evaluating the serum levels of biomarkers (CTX-II for type II collagen degradation and CPII for type II collagen synthesis), histopathological changes (Mankin score, based on the toluidine blue staining of proteoglycans), and immunohistochemical staining of matrix metalloproteinase (MMP)-13 and type II collagen, using a rat experimental osteoarthritis (OA) model. In this review, anterior cruciate ligament transection (ACLT) was performed on the right knee joint to surgically induce OA. Animals were divided into four groups: Control group (Control), sham-operated group (Sham), ACLT group without collagen peptide (ACLT group) and ACLT group with oral administration of CP (CP group). ACLT induced histological damages and significantly increased the Mankin score. However, CP administration markedly suppressed the Mankin score, although this difference was not significant. Moreover, immunohistochemical staining of type II collagen and MMP-13 (an important type II collagen-degrading enzyme) indicated that the amount of

type II collagen increased, whereas the number of MMP-13 positive chondrocytes decreased in the CP group compared with ACLT group.

These observations suggest that CP has the potential to exert chondroprotective action on OA by inhibiting MMP-13 expression and type II collagen degeneration. From the current study, the results indicated that ACLT significantly induced histological damage and increased the Mankin score. However, CP administration substantially suppressed the Mankin score. Serum CTX-II levels were significantly decreased in the CP group compared with the ACLT group, however serum CPII levels did not differ significantly among the four groups. Furthermore, immunohistochemical staining of type II collagen and MMP-13 indicated that the amount of type II collagen was increased, whereas the number of MMP-13 positive chondrocytes was decreased in the CP group compared with the ACLT group. Previous clinical studies have suggested that CP (4.5-10 g/day) has a protective effect on the joints.

### **3.20 A Clinical Evaluation on Long-Term Effectiveness of Polymerized-Type I Collagen Intra-Articular Injections in Symptomatic Knee Osteoarthritis Patients**

Polymerized-type I collagen (polymerized-collagen) is a down regulator of inflammation and a tissue regenerator. The aim was to evaluate the effect of intra-articular injections (IAIs) of polymerized-collagen among patients with symptomatic knee osteoarthritis (OA) in delaying or preventing joint replacement surgery. This was a cohort study of 309 patients with knee OA. Patients with mild-to- moderate disease were treated weekly with IAIs of 2 mL of polymerized-collagen for six weeks (n = 309). Follow-up was for 6-60 months was performed.

The primary endpoints included the following determinations: (1) therapeutic effect; (2) survival from total knee replacement surgery (TKR); (3) Western Ontario and McMaster University Osteoarthritis Index (WOMAC) and pain (visual analogue scale, VAS).

Patients who received IAIs of polymerized-collagen had a statistically significant improvement in the primary criteria (p < 0.05). Kaplan-Meier survival analysis of the therapeutic effect demonstrated 98.8% survival at 60 months



**Table 4. Therapeutic activity of collagen and rosehip extracts in ortho post-surgery**

Sr.no.	PAPER TITLES	YEAR
1	The Anti-Inflammatory Properties Of Rose-Hip.	1999
2	The Effect Of Standardized Herbal Remedy Made From A Subtype Of <i>Rosa Canina</i> In Patients With Osteoarthritis: A Double-Blinded, Randomized, Placebo-Controlled Clinical Trial.	2003
3	An Herbal Remedy, Hyben Vital (Stand. Powder Of A Subspecies Of <i>Rosa Canina</i> Fruits), Reduces Pain And Improves General Wellbeing In Patients With Osteoarthritis-A Double Blinded, Placebo-Controlled, Randomized Trial	2004
4	Collagen-Platelet Composites Improve The Biomechanical Properties Of Healing Anterior Cruciate Ligament Grafts In A Porcine Model: A Controlled Laboratory Study	2009
5	First Clinical Application Of Octacalcium Phosphate Collagen Composite In Human Bone Defect.	2014
6	Concentration Of Vitamin C And Antioxidant Activity Of Rosehip Extracts.	2014
7	One-Step Cartilage Repair In The Knee: Collagen-Covered Micro fracture And Autologous Bone Marrow Concentrate: A Pilot Study.	2015
8	Enhanced Bone Healing Using Collagen Hydroxyapatite Scaffold Implantation In The Treatment Of A Large Multiloculated Mandibular Aneurysmal Bone Cyst In Thoroughbred Filly : Clinical Case Study	2015
9	Efficacy Of Vitamin C Supplementation On Collagen Synthesis And Oxidative Stress After Musculoskeletal Injuries: Systematic Review	2018
10	Pure Type-1 Collagen Application To Third Molar Extraction Socket Reduces Postoperative Pain Score And Duration And Promotes Socket Bone Healing.	2019

with TKR as the endpoint. There was no significant reduction in joint space in any compartment based on the analyzed radiographs. No serious adverse events were recorded. Clinical improvement was defined as a decrease in pain exceeding 20 mm on the VAS and the achievement of at least 20% improvement from baseline with respect to the WOMAC score. Radiographic analysis was performed at baseline.

### 3.21 Reduced Inflammation by the Application of Rose-Hip in Osteoarthritic Patients

Inflammation is often noticeable after surgery and it is the part of healing process. This study includes the anti-inflammatory characteristics of rose-hip. Eight people were involved in the clinical study of anti-inflammatory property of rosehip extract. Four of them were healthy (control group) and the other 4 were diagnosed with osteoarthritis (patient group). The regular consumption of rose hip for 4 weeks showed the decreased serum C-reactive protein levels, and reduced chemotaxis of peripheral blood neutrophils. The anti-inflammatory properties of rose hip can be lucrative in human application as a supplement to reduce inflammation in osteoarthritis and in post orthopedic surgery. The eight people free from other diseases were examined. Four were healthy individuals and the

other four were suffering from osteoarthritis. Their medications included NSAIDs, acetylsalicylic acid, paracetamol and aspirin to relieve pain which had some adverse effects like gastric erosion and kidney disturbances whereas rosehip is totally herbal and with no side effects. The volunteers were initially given high doses (45 g) of rose hip for 4 week, followed by break for 1 month and continuation with low dose (10 g) for next 4 weeks with main meal. The blood was taken from each patient determination of CRP levels and chemotaxis. CRP is a vital regulator of inflammation. Lower CRP levels indicate lower inflammation. There was decrease in CRP levels in high and low dose than no therapy. The reduced peripheral blood neutrophil chemotaxis was observed. Its anti-inflammatory, analgesic property, low cost and easy administration make it ideal as an alternative to other drugs. It can be efficiently used for the treatment of osteoarthritis patients.

### 3.22 Placebo Controlled Study of Rose Hip Powder in Alleviating Pain Due To Osteoarthritis

Standardized rose hip powder extracted from the fruits of *Rosa canina* was used in alleviating pain in osteoarthritic patients. The main objective of this study was to determine the effect of rose hip powder on hip joint movement, knee joint movement and activities of daily living (ADLs) of

osteoarthritic patients. It was a blinded study, which included 100 patients divided in 2 groups. The treatment group was given 0.5 g standardized rose hip capsule for 4 weeks and the placebo group was given placebo capsules of same taste, smell and appearance as rose hip. Knee and hip movement was monitored in both the groups before and after the trial. In treatment group there was substantial advancement in the hip joint and knee joint movement and the pain was decreased. Conclusion: The rose hip powder does not have any adverse effects like the NSAIDs and other medications. In this study 64% patients reported reduced pain and improvement in knee movement and hip flexion was observed. There is a need of placebo control in investigating the effect of natural herb. The open study does not give only the results of new remedy but also the patient's perceptions. Therefore the placebo effect should be deducted to get prominent results. All the patients diagnosed with osteoarthritis were examined radiographically 12 months before the study. Two groups of 50 patients were divided, the treatment group was given 0.5 g rose hip capsule while the placebo group was administered with placebo. The standard values of hip flexion, knee flexion and for external- internal hip rotation are 125°, 140° and 40° respectively. Among 100 patients some had hip issues while others had knee problems. After the 4 months of treatment, patients administered with standardized rose hip powder experienced improved hip flexion, external and internal rotation. On other hand the placebo group showed substantial improvement in passive hip flexion but not in internal and external rotation. 64% of patients administered with rose hip powder reported complete pain relief but the 35.4% reported no relief. In the placebo group 56.3% patients had no effect whereas the other 43.8% had reported slight improvement. All the patients were told to continue their dose of NSAIDs during the trial. It was found that 7 patients in patients group lowered their NSAIDs consumption and none other increased, while in placebo group 4 patients increased their dose and 3 patients reduced the consumption. In 2 patients moderate gastrointestinal discomfort was reported. No significant changes were observed in difficulty in performing ADLs in both the groups. Through this study we found that the compliance was 98% in treatment group and 96% in placebo group. The hip movement had improved in treatment group contrast to placebo group placebo group. The impact on ADLs remained unaffected I both the groups. Majority of patients experienced

reduction in pain. Therefore this study suggests the effective use of rosehip powder in treatment of osteoarthritis.

### **3.23 A Double Blinded, Placebo-Controlled, Randomized Trial of Rose Hip Powder In Patients With Osteoarthritis**

The main objective of this study is to examine the effect of Hyben vital (An herbal remedy made from subspecies of *Rosa canina*) to reduce stiffness, pain and inflammation. This is a double blinded, placebo-controlled crossover study. 112 patients with osteoarthritis volunteered for this study. Half of them were given placebo for first 3 months and then Hyben vital for next 3 months and the other half vice -versa. The examined effects on joint pain, stiffness and general wellbeing were recorded in a personal diary. Group A (placebo first) reported more progress by Hyben vital compared to placebo. Group B (Hyben vital first) reported same effects from both medications. This could be due to the "carryover" effect of Hyben vital. Hyben vital was examined for 2 primary effects; joint pain and effect of alteration of medication. The secondary parameters analyzed were joint stiffness, general wellbeing; mood, energy and sleep quality and choice of one drug over another. The drug administered daily was 0.5 g capsules 2 times a day for three months, Followed by change in medication for next three months. Out of 112 volunteers 71 were women and 41 men. To get precise results patients were segregated according to the demographic and osteoarthritic characteristics. For the further analysis 80 patients were left after some patients discontinuing the trial. In group A (placebo first) substantial difference was observed in favour of Hyben vital. 25% of improvement in pain was seen earlier followed by 50 % improvement by Hyben vital. In group B (Hyben vital first) no difference was observed between the effects of both drugs.  $1.45 \pm 1.28$  for active treatment and  $1.72 \pm 1.37$  for placebo were determined. The crossover effect could be the possible explanation in this case. The stiffness in joint was analyzed on a scale of 0 (being no improvement) to 4 (almost complete relief from stiffness). The effect was same as observed in pain. In case of general wellbeing criterias, similar results of high difference in group A and indistinguishable results in group B were observed. The changes were in favor of active treatment in placebo group. The reports for preference of medicine again showed significant difference in group A;

24 patients preferred Hyben vital, 8 preferred placebo over Hyben vital and the remaining 9 were not sure. In group B 12 patients opted for Hyben vital whereas 20 patients voted for placebo treatment and 8 did not have any opinion. The herbal remedy of rose hip was found effective in reducing pain and stiffness along with maintaining general wellbeing of the patient without any adverse effects. So we can rely on rose hip powder for reducing osteoarthritic pain.

### **3.24 Improved Healing of Anterior Cruciate Ligament Post Reconstruction by Platelet-Collagen Sponge: A Controlled Laboratory Study**

The main objective of the study is to answer the question; Can collagen-platelet composite (CPC) enhance the mechanical and structural properties of ACL and postoperative decrease the knee laxity? Fourteen immature, 30kg Yorkshire female pigs were involved in the study. They underwent ACL reconstruction surgery with an allograft; 7 went through standard ACL allograft surgery (ACLR; control) and other 7 experienced collagen-platelet composite enhanced allograft reconstruction (E-ACLR; Experimental). 1 pig from control group was euthanized during trials due to condylar fracture. 15 weeks later all the pigs were euthanized. Followed by measuring anterior-posterior (AP) knee laxity and structural properties. The current treatment of ACL tear includes reconstruction with allograft or autografts which increases knee laxity and persists till the age of graft. So as an alternative to this method CPC enhanced allograft was used. In the E-ACLR the CPC was threaded in the allograft which reduced postoperative knee laxity and improved structural properties in a porcine model after 15 weeks. The porcine model is felicitous as it has same hematological properties as humans which are important for studying platelets. It also has anatomical resemblance to humans and other big animal models. To make the collagen-platelet composite; blood was withdrawn from the pigs. It was suspended in tubes containing sodium-citrate solution followed by centrifugation. The supernatant was obtained which was again centrifuged to obtain platelet pellet. The 5 times high concentrated platelet pellet was extracted. The collagen sponge was made from bovine fascia, which passed through various processes. The sponge was dipped in platelet, the resulting sponge was freeze stored under

vacuum until use. 13 pigs underwent the reconstruction surgery. Standard allograft reconstruction as performed on 6 pigs, while on 7 CPC enhanced ACL reconstruction was demonstrated. Freshly-frozen allografts were obtained from similar donor pigs. The allograft in the control group was fixed in the femoral and tibial tunnel with the help of bio absorbable screw. In the experimental group collagen-platelet composite sponge was threaded along with the graft and fixed in the osseous tunnels. Subcuticular stitches were used to close the incision. Just before euthanasia MRI scanning was done. In conjunction with MRI protocols clinical examination was conducted. It included study of minimum extension angle, flexion angle, and total range of motion (ROM) followed by Lachman test. The mechanical tests included AP laxity and tensile failure testing. The AP laxity values were reduced by 28% and 57% for 60° and 90° for knee flexion respectively. Maximum improvement in failure load (approx. 60%) in experimental group than in control group was recorded. After biomechanical testing the dissected graft was kept in formalin for 7 days followed by cutting it in cross-section and embedded in paraffin. Qualitative examination was done by placing it on glass slides stained with hematoxylin and eosin. The statistical and biomechanical studies suggested structural improvement in E-ACLR group and knee laxity was reduced. Improvements in normalized yield load and normalized failure load was resulted in E-ACLR group. Not a single animal had any post-operative complication or any adverse effect was not observed. All animals were able to handle the weight in 12 hours and were able to walk within a week. The evaluation of CPC application to ACL reconstruction showed no difference in linear stiffness and AP laxity was observed at 30° flexion in both groups. However significant reduction in AP knee laxity was determined and improvement in structural features were noted. The CPC administered ACL reconstruction was efficient in enhancing post-operative healing and augmentation in structural characteristics.

### **3.25 Enhanced Bone Regeneration by Collagen and Octacalcium Phosphate Combination**

The study is based on the preceding demonstration of octacalcium phosphate and collagen mixture which encouraged bone regeneration in bone defect in a rodent or a canine model. This study focuses on the bone

regeneration capability of OCP/collage in humans. Two patients who had radicular cyst or apical periodontitis were endorsed for clinical study. Radiographic study and CT examination was conducted for regular time intervals. The OCP/collagen discs were prepared for implanting in the bone defect. The studies showed the effective bone healing at 3 and 6 months. The post-operative phase of bone healing was normal and showed no allergic or immune reactions. It indicated that the OCP/collagen can be used in human bone defects for rapid bone regeneration. Remodeling of large bones after the removal of defected bone or cyst is challenging in orthopedics. OCP is considered to be precursor for apatites like dentin, enamel and bone. Crystal structure of OCP impedes its molding, to upgrade its handling it is combined with collagen. Their combination intensifies the bone healing property post-surgery. The past medical record of the patients was regular. In both cases no post-operative complications were observed. The cystectomy was followed by OCP/collagen disc implantation with no after effects. 1 day after there was upsurge in C-reactive protein which came to initial levels after 7 days. The pain in the operative are was regulated by painkiller. The study suggests the lucrative and safe use of OCP/collagen post cystectomy. The radiographical studies showed the increment in radiopacity. The CT examination revealed the increase in radiopacity from 3 months to 6 months. OCP/collagen transforms in to apatite crystals post-surgery. The radiopacity indicates the new bone formation. The OCP/collagen therefore can be used for effective and enhanced bone regeneration in post-orthopedic surgeries.

### 3.26 Efficacy of Rosehip Extraction as Vitamin C Supplementation

Rosehip is extracted from the fruits of *Rosa canina L.* They are said to have high antioxidant property and rich in vitamin C. the main aim of this paper is to determine the antioxidant property and the vitamin C content in the different parts of the fruit: seeds, skin and pappi. The raw material was crushed and segregated into its different parts. Extraction was carried out in magnetic stirrer under continuous agitation. The vitamin C concentration, antioxidant property and calorific value were analyzed by different chemical tests and methods. The study verified the high vitamin C content especially in skin. Seeds have high oil composition; hence it can be used in oil for cosmetic applications. Pappi had high calorific value, so it can be used as a solid

fuel substitute. The extract can be effectively used as vitamin C supplements. Many experimental studies have shown that the rose hip has large amount of ascorbic acid (vitamin C) i.e. approximately 6 times more than in orange. The fruit parts were segregated in order to determine antioxidant property and vitamin C content in different parts. The dried raw material was milled before fractionation, followed by extraction by continuous agitation in magnetic stirrer or thermostatic shaker. For 1 part of plant material 10 parts of solvent was added to eliminate the solubility limitations. Gravimetric analysis of rose hip showed highest percentage of seeds followed by skin and pappi (Table 1). Vitamin C was determined by titration of infusion of rosehip (prepared by boiling in water) with 0.05 M iodine using starch as indicator. Highest concentration was found in skin and lowest in pappi (Table 2). Antioxidant capacity (AOC) was examined by DDPH method which is antioxidant assay based on electron transfer that changes the color to violet. AOC is expressed by factor IC<sub>50</sub>%, which is inversely proportional to antioxidant capacity. The skin had highest AOC followed whole fruit extract (Table 3). Calorific value of pappi was also determined by a calorimetric device. As it has high thermal energy it can be used as solid fuel pellets. The fractionation of this fruit helps in getting different activities which are economical and extremely reliable for human use. This can be used as antioxidant, in cosmetics and especially as a vitamin C supplement.

**Table 5.1. Gravimetric analysis of rose hip**

Fraction	% of whole fruit
Seeds	57.6
Skin	36.5
Pappi	5.9

**Table 5.2. Vitamin C concentration in different parts of rosehip**

Fraction	Vitamin C content (mg/g)
Whole fruit	1.1
Skin	2.3
Seed	0.4
Pappi	0.2

**Table 5.3. Antioxidant activity of rosehip**

Fraction	Antioxidant capacity (IC <sub>50</sub> % ml/l)
Whole fruit	2.59
Skin	2.05
Seeds	20.41

### **3.27 Effectiveness of Collagen-Covered Micro fracture And Bone Marrow Concentrate Composite in Knee Cartilage Repair: A Pilot Study**

There are various techniques for the treatment of focal cartilage defects. The limitations of these techniques include no long term functional improvements, high priced techniques and two operations of autologous chondrocyte implantation. This has convinced for a need of a better and single step cartilage repair method having histological and clinical evidences. Nine patients diagnosed with focal cartilage defects were treated with collagen-covered micro fracture and bone marrow concentrate (C-CMBMC). 1 patient however pulled back due to clinical improvement. The trial was conducted for 12 months. Histological studies revealed different type of repairs. This clinical trial proved to be efficacious in treatment of focal lesions of the condylar articular cartilage by the application of C-CMBMC. This study reveals its safe application and improvement in post-operative knee function. This method emphasizes on cartilage recreational ability by C-CMBMC. The BMC was extracted from iliac crest as it contains higher amount of mesenchymal stem cells and high doubling potential. The exact shape of defect was determined by using a template. The collagen was cut in same shape and immersed in BMC until use. When water flowing stopped; excess water was removed by suction. Using a long needle fibrin glue and BMC mix was applied followed by positioning the membrane and applying more fibrin glue and BMC mix over it. It was allowed to dry and excess of the glue mixture was removed. 4 patients volunteered in second-look arthroscopy and biopsy harvest. The specimen was analyzed using International Cartilage Repair Society Cartilage Repair Assessment (ICRS CRA). The histological studies according to ICRS II score revealed that in 1 patient hyaline cartilage was found, fibrocartilage was found in 2 cases and mixture of both hyaline and fibrocartilage was found in other patient. In all cases the collagen was reabsorbed proving its biodegradability. All patients were clearly declared as normal according to arthroscopic evaluation as per ICRS CRA. Patients were retrospectively analyzed according to various standardized outcome assessment tools and MRI scans. All the patients in this study reported significant improvement which was analyzed by different assessment tools and MRI scans. The MRI scans disclosed

the bone marrow edema and subchondral plate irregularities. However it also revealed complete filling of defects in all the cases. Regeneration of hyaline cartilage and fibrocartilage was seen arthroscopically. Briefly this clinical and histological study suggested that the procedure was safe to use and provided short term pain relief and enhanced functional ability by Collagen-Covered Microfracture and Bone Marrow Concentrate.

### **3.28 Post-Surgical Bone Healing By Collagen Hydroxyapatite Scaffold Implantation: A Clinical Case Study**

Autografts, allograft and xenografts are used for reimplantation in segmented bone defects, tumors, cysts, etc. The autografts are the bone tissue taken from the patient's own body and reimplanted it causes impediment in large defects whereas allograft is the bone tissue taken from cadaver or the donor which sets the drawback of immune reactions. The biodegradable, biocompatible and bone graft tissue capable of osteogenesis in body was required. The collagen-hydroxyapatite (CHA) is used as bone graft substitute material in a 2 year old thoroughbred filly (female horse of pure breed) diagnosed with multilobulated aneurysmal bone cyst. The post-operative tests were conducted at 2 weeks and 3, 6 and 14 months after treatment with CHA-scaffold. After 14 months it was found that the compact bone was remodelled, the enlargement in mandible was reduced with no fluid filled cavity, with clearly distinct medulla and cortex. This indicated the conducive outcome and its promising application as bone graft substitution for enhancing bone repair and lucrative in human applications too. A 2 year old thoroughbred filly was found having a large swelling in the right mandible, no apparent pain was experienced. It was diagnosed with multilobulated mandibular bone cyst with tooth displacement, distortion and hypoplasia. CHA scaffold was fabricated using freeze drying technique. The mare was desensitized followed by removal of the cystic and defected bone via a 20 cm long skin incision. To boost the bone healing 5 CHA scaffold sheets were placed alongside the mandible. Totally repaired surgical wound was found at second week evaluation. 3 months post-surgery the operated mandible was contracted and the cavity was filled with moderately dense mineralized tissue. Slight growth was observed in tooth buds surrounding the cyst. The distortion and displacement was comparatively less. The 6 months assessments

showed no masticatory complication. The mandible had diminished in size in contrast to third month. The fluid-filled area was taken over by moderately dense mineralized tissue. The advantageous application of CHA scaffold was demonstrated in the study. The absolute intracystic injection was proved to be effective in aneurysmal bone cyst although it was considered as perilous due to closeness of mandibular nerves and tooth roots. So the CHA scaffold was devised as an alternative, it had impressive properties such as biocompatibility, biodegradability and osteogenesis in human body. This study involves the removal of the bone tissue followed by the implantation of scaffold to enhance the repair of the bone. Such combination of process was never applied previously to remove large cyst. The biodegradability and resorption ability was proved by the CT images taken after 3 months which showed zero trace of collagen scaffold. This approach of enhanced bone healing without supplementary growth factors like BMP has proved efficient bone graft substitute and fit for human use.

### **3.29 Increased Collagen Synthesis Post Injury by Vitamin C: A Systematic Review**

Various studies on biochemical pathways reveal the successful effect of vitamin C in enhanced collagen synthesis and soft tissue healing. Methodology: This is a systematic review. The preclinical studies showed the enhanced bone healing in vitamin C supplementation group than in control groups. The other studies demonstrated effective tendon healing, type-I collagen synthesis and improvement in anterior cruciate ligament (ACL) graft incorporation. Through various studies Vitamin C has proved to be efficient in bone healing after injury, lowering the oxidative stress and elevating type-I collagen levels. Throughout the study no side effects were observed in both animal and human trials. Therefore vitamin C can be used as a supplement for collagen synthesis. Collagen synthesis and cross-linking is crucial for healing tendons, ligaments and bones. The study of biochemical pathways through different articles has shown that the vitamin C is responsible for augmented collagen synthesis. Additionally collagen shows antioxidant properties. Initially 286 articles were selected after examining and screening 10 articles which were precise were accepted for the review. In the preclinical studies the vitamin C dosage were based on

animal weight and in some it was kept standard. The duration of trials was 3 to 6 weeks. Some studies allowed standard diet, some did not contain vitamin C in their diet and the others had no restrictions. Some studies allowed animals to move freely while some immobilized the injured part. Out of 4 studies 3 suggested accelerated collagen synthesis resulting in bone healing compared to control groups. The other study reported no significant difference compared to control group. And the remaining studies reported in increase graft healing and antioxidant effects of vitamin C. Not a single study reported adverse effects. The efficacy of vitamin C on lowering oxidative stress was reported; 3 studies showed reduced oxidative stress whereas 1 study reported its opposing effect. Amongst 3 clinical studies 2 focused on supplementation of vitamin C and other antioxidants while the 1 study analyzed vitamin C solely. The dosage varied from 60 mg twice daily to 500 mg twice daily. Two studies evaluated bone healing while the other demonstrated muscle healing and antioxidant effect after ACLR. Clinical trial demonstrating muscle healing reported no significant difference in treatment and control groups, while the other two clinical trials were contradictory, where 1 showed no difference between control group and treatment group and other reported efficient bone healing. But no adverse effect was reported in single clinical trial. The systematic review provides the clear preclinical evidence of efficient bone healing by vitamin C consumption. However the clinical trials were conflicting. Overall 4 out of 5 studies reported stimulation of biochemical pathways related to collagen synthesis which resulted in increase of collagen synthesis. No adverse effect was reported in animals as well as humans. Therefore we can conclude that vitamin C can be used to increase collagen in vivo. And more clinical trials should be conducted to investigate accelerated bone healing effect of vitamin C.

### **3.30 Elevation in Socket Bone Healing after Third Molar Extraction Surgery by Pure Type-I Collagen**

The extraction of 3<sup>rd</sup> molar is very usual due to orthodontic reasons in dentofacial orthopedics. This study examines the effect of pure type-I collagen in 3<sup>rd</sup> molar extraction to reduce postoperative complexities and enhance the socket bone healing. 14 patients were involved in the study who wanted to remove the 3<sup>rd</sup> molars. One of the socket was filled with pure type-I collagen (experimental group) and other socket

was kept empty, and blood clot was formed (control group). At 1, 2, 4 and 8 weeks after tooth extraction the postoperative pain score, duration, mouth-opening limitation and socket bone healing was analyzed. The successful application of pure type-I collagen in lowering the intensity of pain score and duration, curtailing the mouth-opening limitation and augmented socket bone healing in the experimental group. The filling of socket with pure type-I collagen resulted in blood clot stabilization which restrains from inflammation and infection, diminished complications after the surgery, and new tissue generation. The 3<sup>rd</sup> molars were extracted and one was filled with pure type-I collagen (experimental group) and other was left unloaded (control group) which was undisclosed to the patients. At 1<sup>st</sup>, 2<sup>nd</sup>, 4<sup>th</sup> and 8<sup>th</sup> week the radiographical analysis was done. The 1 week study examined that the experimental group had lower mean pain score ( $2.6 \pm 1.2$ ) than control group ( $4.7 \pm 2.0$ ), it also revealed the considerable decline in pain duration after operation in experimental group ( $2.7 \pm 1.4$  days) than control group ( $3.7 \pm 1.8$  days). Clear difference was noted in trismus, experimental group (45%) and control group (90%). The extraction force and operation-

induced pain was also determined. The examination of pocket dept of disto-buccal line-angle of the second molar prior to operation and after 1, 2, 4 and 8 weeks showed lesser depth at experimental site than at control site. The type-I collagen has proved to be efficient in preventing the inflammation, infection, hematoma and alveolar osteitis at the site of operation. This detailed analysis indicated the application of pure type-I collagen at 3<sup>rd</sup> molar extraction socket lessen the postoperative pain score, duration, mouth-opening limitation (trismus) and increase in mineralization of bone at site of operation and collagen proved to be biocompatible.

### 3.31 Standardized Rosehip Powder as a Natural and Alternative Cure For Patients Suffering from Hip and Knee Osteoarthritis

Arthritis is a medical condition which causes swelling and inflammation of the body joints. Patients primarily consume chemical and synthetic drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids to overcome the osteoarthritic pain.

**Table 6. Therapeutic activity of collagen and rosehip extracts in ortho post-surgery**

Sr. No.	Paper Title	Year
1	The effects of a Standardized Herbal Remedy made from a subtype of <i>Rosa canina</i> in patients with Osteoarthritis: A Double-Blind, Randomized, Placebo-Controlled Clinical Trial	2003
2	A herbal remedy. Hyben Vital (stand. Powder of a subspecies of <i>Rosa canina</i> fruits), reduces pain and improves general wellbeing in patients with osteoarthritis-- a double-blind, placebo-controlled, randomised trial.	2004
3	A Powder made from seeds and shells of a rosehip subspecies ( <i>Rosa canina</i> ) reduces symptoms of knee and hip osteoarthritis: A randomized, double-blinded, placebo controlled clinical trial	2005
4	Autologous Chondrocyte implantation in Chondral Defects of the Knee with a Type I/III Collagen Membrane: A Prospective Study with a 3-Year follow up	2007
5	The effect of rosehip ( <i>Rosa canina</i> ) on plasma antioxidative activity and C-reactive protein in patients with rheumatoid arthritis and normal controls: a prospective cohort study	2011
6	The Collagen component of biological bone graft substitutes promotes ectopic bone formation by human mesenchymal stem cells	2013
7	Comparing different preparations and doses of rosehip powder in patients with osteoarthritis of the knee: An exploratory randomized active controlled trial	2014
8	A New Bioinspired collagen-hydroxyapatite bone graft substitute in adult scoliosis surgery: Results at 3-year follow up	2017
9	Effects of Collagen- $\beta$ Tricalcium Phosphate bone graft to regenerate bone in critically sized rabbit calvarial defects	2019
10	Changes in Periprosthetic bone mineral density and bone turnover markers after Osseo integrated implant surgery: A cohort study of 20 trans femoral amputees with 30-month follow up.	2019

The subspecies of the genus *Rosa canina* are rich in phenolic and polyphenolic compounds which known to exhibit antioxidant, anti-inflammatory and anticarcinogenic effects. The latter is also renowned for its protective action against the development of any human diseases. In this study, approximately one hundred patients suffering from either hip (44 patients) or knee (56 patients) osteoarthritis were considered. Patients were randomly divided into two treatment groups, with each group containing 50 patients. The patients under the first group were supplemented with capsules containing 0.5 grams of standardized rose hip powder. While the latter was supplemented with placebo capsules. Both the groups had to consume the capsules twice a day for a duration of four months. Statistical tools such as Mann-Whitney test and Wilcoxon rank test was used to assess the results obtained from the two groups. Based on the results obtained, it can be concluded the standardized rosehip powder was able to effectively reduce the various symptoms and pain experienced by approximately 64.6% of patients. Moreover, a higher degree of improvement in the different types of movement was observed for patients under the test group.

Patients under the test group, whose diet was supplemented with standardized rosehip powder (SRHP) exhibited a significant decrease in the pain experienced during the course of study. The percentage of improvement in passive hip flexion, external rotation and internal rotation was found to be 40%, 17.1% and 35% respectively.

The efficacy of the standardized herbal powder was proved by the degree of hip and knee movement along with the reduced levels of pain experienced by the patients. Thus, indicative that the herbal powder composition can serve as an alternative and natural remedy for the treatment of osteoarthritis. However, it is to be noted that the movement and attachment of the hip and knee joint varies from each other [41,42]. The hip joint is similar to a ball and socket joint, in which the femoral head attaches to the acetabular rim of the pelvis. Whereas, the knee joint is a hinge type synovial joint, in which the femur interacts with the tibia and forms the main knee joint.

### **3.32 A Standardized Herbal Powder, Hyben Vital to Ameliorate the Pain and Swelling in Patient's Suffering from Osteoarthritis**

Osteoarthritis is a condition which arises as a result of gradual shearing stress on the cartilage,

and causes inflammation leading to pain and discomfort. Patients consume non-steroidal anti-inflammatory and glucocorticoids drugs such as ibuprofen and dexamethasone respectively to ameliorate the pain. However, the recurrent use of these pain-relieving drugs can cause long term side-effects on the body such as—gastrointestinal, cardiovascular, hepatic complications. To circumvent the above-mentioned impediments, researches are exploring alternative medications or supplements which will help these osteoarthritic patients. The main objective of this study is to analyze the efficacy of herbal rosehip powder commercially sold under the name of Hyben Vital. In total 112 patients suffering from arthritis of various joints, had participated for this study. The important criteria considered for the trial are-- changes in joint pain and alterations in the pain-relieving medications. The patients were randomly divided in to two groups A and B which comprises of 47 and 50 patients respectively. The trial was divided into three periods in which, initial 2 weeks was the run-in period followed by the allocation of two successive treatment procedures for a duration of three months each. The former period was mainly devised to familiarize the patients with the trial routine. While in the latter period, the two treatment protocols which were followed for this study include, Hyben Vital capsules (herbal powder) and an identical placebo capsule. Statistical tools, such as the Wilcoxon's test and Mann-Whitney test was applied. The former test was used to detect the similar pairs within the clinical trial. While the latter was used for conducting comparative analysis. Therefore, the Group B patients (initially on Hyben Vital capsules) exhibited an improved treatment than the Group A patients. It can be concluded that the herbal remedy composed of rosehip powder was able to effectively reduce the symptoms of pain and discomfort in patients suffering from osteoarthritis.

For the data obtained, it was understood that for the initial 3 months group A were placed on placebo capsules followed by Hyben Vital capsules and the reverse protocol was followed for group B patients. The values of group B patients were found to be 0.60, 0.38 and 0.14 respectively, which was much higher than the values of group A patients. Initially for this clinical trial a total of 125 patients had participated. However, due to unforeseen circumstances such as patient related issues, protocol violation or due to consumption of higher dosage of steroids many patients had to withdraw mid-way.



Towards the end of the trial only 85 patients had completed

### **3.33 A Random Placebo Controlled Clinical Trial to Assess Efficacy of Rosehip Powder Prepared Using Seeds and Shells**

Osteoarthritis is a condition which primarily targets the joints of the body. Conventional treatment options for the treatment of osteoarthritis mainly include the consumption of oral analgesics and topical pain medicine including non-steroidal anti-inflammatory drugs (NSAIDs). However, the use of alternative and complementary medications is highly preferable. The primary objective of this study is to evaluate whether subspecies of the herbal powder, *Rosa canina* might reduce symptoms and pain experienced by osteoarthritic patients. In this study, randomly a total of 94 patients over the age 35 years, suffering from hip or knee osteoarthritis were selected. The patients were divided into two groups and placed on two different modes of treatment, that is Active treatment (n=47) and Placebo treatment (n=47). The diet of patients receiving active treatment was supplemented with 5g of the herbal powder. While the patients in the other group were receiving placebo. The clinical trial comprises of three consecutive rounds, commencing with a 3-week period followed by two subsequent 3-month treatment period. Towards the end of every treatment period the patients were evaluated on the basis of Western Ontario and McMaster Universities (WOMAC) questionnaires. Thus, it can be concluded that the standardized herbal rosehip powder was found to be effective towards the patients suffering from knee and hip osteoarthritis. However, further investigations are required to ascertain the specificity and the biological activity of the various subspecies of *Rosa canina*. The inclusion of rosehip powder in comparison to placebo as a daily supplement in the diet exhibited an exceptional reduction the pain experienced by the patients. Over the three phases of the trial starting from three weeks to three months, the symptom score was found to be  $p < 0.018$ ,  $p < 0.038$  and  $p < 0.035$  respectively. Approximately 82% of patients reported a reduction in pain within first three weeks of active treatment.

### **3.34 Autologous Chondrocyte Implantation in Chondral Defects- With a Type I/II Collagen Membrane**

In this study, autologous chondrocyte implantation technique was adopted for the

treatment of chondral defects of the knee. Autologous Chondrocyte Implantation (ACI), promotes the restoration of the native connective tissue, hyaline cartilage via the implantation of cartilage cells. A total of 63 patients (31 males and 32 females) suffering from chondral deformities underwent an autologous chondral implantation procedure. The patients were divided into three groups on the basis of the localization of deformity that is femoral condyles, trochlea and retro-patellar region of the knee. A bilayer porcine collagen type I and type II membrane was used as a protective sheath over the suspension of cultivated chondrocytes, at the site of defect. This membrane was mainly considered due since it has two distinct surfaces, an external surface which serves as a protective barrier and an internal porous surface which promotes the growth and production of cartilage specific molecules. The International cartilage repair society (ICRS) and the Cincinnati scoring system was used to evaluate the regenerative capability of cartilage repair. All the patients were categorized into three groups and were under observation from pre-operation to 6-, 18- and 36-months post-surgical procedure. Thus, in the implantation of autologous chondrocytes, cartilaginous membrane can successfully replace periosteous flaps to treat of chondral defects. Since, it is able to improve the quality of life of the patient after surgery and at the same time has also reduced the total time required for completion of the implantation operation. An exceptional increase in the values were obtained during the period of pre-operation and post operation. The tissue repair was found to be durable and long lasting even after 2 years of the surgery and demonstrated stable results for approximately 5 to 11 years. On the contrary, the study conducted did not include a randomized control group of patients.

### **3.35 Effects of Rosehip Powder on Plasma Anti Oxidative Activity and C - Reactive Protein in Patients with Rheumatoid Arthritis**

Rheumatoid arthritis (RA) is an autoimmune condition leading to inflammation of joints and connective tissues. Patients suffering from RA consume drugs such as, non-steroidal anti-inflammatory drugs (NSAIDs), disease modifying anti-rheumatic drugs which are mainly associated with multiple side effects. As a result, there is trend towards the use of alternative and complementary remedies for treatment of RA. *Rosa canina* commonly also

known as rosehip powder, is an old herbal remedy rich in nutrients and imparts multiple health benefits. Rosehip powder contains fatty acids such as palmitic, linoleic and  $\alpha$ -linoleic acid. The main aim of this study is to evaluate whether the inclusion of rosehip powder in daily diet would affect the C-reactive protein (CRP) level and to assess the antioxidant enzyme activity. The experimental study was performed for four weeks and included 20 female patients suffering with RA and 10 females under the control group. From both the groups, the patient's diet was supplemented with 10.5grams of rosehip powder. Towards the end of the study blood samples was collected in tubes containing EDTA as an anticoagulant. Based on the results, it can be concluded that the inclusion of 10.5 grams of rosehip powder as a supplement did not affect either of the groups. There was neither an increase nor a decrease in the levels of inflammatory marker, CRP or the antioxidant enzymes. For standard plasma level of the inflammation marker CRP, no significant difference was noted. Similar results were obtained in case of the antioxidant enzyme activity as well the tools used for measurement of the outcome values. The results obtained from this study stand contradictory to the results of another study, in which the intake of rosehip powder (45g) lead to decrease in the CRP values. The other study was performed on patients suffering from osteoarthritis whereas in this study, patients included were primarily suffering from rheumatoid arthritis. Theoretically, it was expected that due to inflammation there may be an elevation in the concentration of reactive oxygen species or reactive nitrogen species thereby affecting the antioxidant activity of the enzyme.

### **3.36 Use of Collagen in Bone Graft Substitute to Promote Ectopic Bone Formation by Mesenchymal Stem Cells**

Bone grafting procedures is mainly performed in cases of patients suffering from bone disorders. Bone substitutes can be broadly classified into the following categories—autograft, allograft and xenograft. The latter, xenograft is most preferable alternative since it is cheap but on the contrary the results obtained are highly variable. Recently the use of biological ceramics such as  $\beta$ -tricalcium phosphate or hydroxyapatite as synthetic bone substitutes are on a rise. The primary objective of this study is to determine whether xenogeneic bone graft substitutes will

support the genesis of new bone. This can be achieved by the process of bone tissue engineering which involves the fusion of biomaterials with mesenchymal stem cells (MSCs). In the first half of the study, MSCs were harvested from 9 patients undergoing hip replacement or bone reconstruction surgery. Subsequently, to promote in-vitro osteogenic, adipogenic or chondrogenic differentiation the harvested cells were seeded in an osteogenic, adipogenic or chondrogenic nutritive medium, respectively. While, in the second half, involves the production of biomaterial/MSC construct for performing in-vivo studies. In total 5 bone graft substitutes (BGS) were used out of which 4 BGS were mainly procured from equine and bovine origin, with and without collagen (bHA-C, bHA, eHA-C and e-HA). These constructs were further implanted in severe combined immunodeficient mice. To assess the role of collagen in the genesis of new bone, a quantitative histological examination called histomorphometry was performed. Thus, from the results obtained it can be concluded that the rate of formation of ectopic bones was observed to be higher with collagen containing BGS. The formation of Nano pores was found to be highly conserved in biological materials such as bHA, eHA-C and eHA. In addition, biomaterials containing collagen as an additional component exhibited higher frequency of bone formation. The inclusion of a natural biological component, collagen into the experiment protocol demonstrated a higher capacity of osteogenic activity of MSCs. The presence of collagen fibers amplifies the process of cell attachment, proliferation as well as migration of progenitor cells. In addition, it also encouraged bone deposition thus accelerating the genesis of new bone.

### **3.37 Use of Variable Composition and Dosage of Rosehip Extracts on Patients with Knee Osteoarthritis**

Osteoarthritis is a condition which primarily targets the joints of the body. Conventional treatment options for the treatment of osteoarthritis mainly include the consumption of oral analgesics and topical pain medicine including non-steroidal anti-inflammatory drugs. Lately, there has been a surge in the use of nutraceutical products as an alternative medication. On the basis of previous studies, subspecies of *Rosa canina* has proved to serve as an effective alternative for treatment of infections and inflammatory disorders. The aim of this study was to demonstrate and analyze the

effectiveness and safety of rose hip powder of variable composition and dosage. A 12-week random clinical trial was conducted, comprising of a total of 150 patients suffering from knee osteoarthritis. The patients were categorized into 3 groups on the basis of the variable dosage and the composition. The first group of patients consumed 6 capsules of original powder daily. While the second and third groups consumed six capsules and three capsules of enhanced rose hip powder per day, respectively. The enhanced powder was mainly prepared using rosehip peels while, the original powder comprises of fleshy peels with the seeds. The primary outcome was measured using a knee specific scale, Knee Injury and Osteoarthritis Outcome Score (KOOS). The improved powder has proved as effective as the original powder, even in three capsules. The results obtained was indicative that the severity of the symptoms was reduced when three capsules of enhanced rose hip powder was included in the daily diet of the patient. On the basis of the values obtained, a difference of 5.97 was noted between the efficacy of the original and the improved composition of the rosehip powder. In addition, patients who consumed six capsules per day, the refinement in their lifestyle observed.

### **3.38 A Clinical Study Based on Use of Collagen-Hydroxyapatite Bone Graft as a substitute for Adult Scoliosis Surgery**

The malformation of the spinal cord at an angle more than 10 degrees results in the development of a condition, adult scoliosis. Spinal cord defects can cause discomfort and debilitating conditions associated with segment degeneration and sagittal imbalance. Autologous Iliac crest bone graft is viewed as the most effective mode of treatment. However, given its limited availability and increased morbidity at the harvest site, is not preferable. In this study the use of ceramic biomaterials fused with used as a bone graft substitute for treatment of adult scoliosis and to obtain a longer posterolateral fusion. The interaction between inorganic and organic biomaterial, hydroxyapatite and type I collagen (MHA/Coll) respectively, is a highly regulated process. Furthermore, magnesium ions were used as doping ions as they enhance the process of new bone formation. In total 41 patients were enrolled for the clinical study and the average body mass index was calculated to be 24.5. In case of the surgical procedure two approaches were adopted, posterolateral fusion

and a transforaminal approach to the intravertebral disc space was performed. The latter approach was performed for only 13 patients, in which the local bone was placed in the anterior portion of the interbody space. The Lenke Classification system was used for radiological evaluation of the spinal fusion.

After 6 months, majority of the patients had attained a fair degree of arthrodesis and only one patient exhibited no fusion. By the end of 12 months, approximately 56% of the patients had successfully attained grade A of the Lenke Classification system. In the downside 2 patients demonstrated poor to moderate degree of spinal fusion (grade C). By the end of 36 months, majority of the patients either exhibited grade A or grade B level of spinal fusion. Due to the rising complications associated with the harvesting of autologous bone graft from the iliac crest, the application of synthetic bone graft substitute is more favoured. The results obtained from the study is suggestive that the application of MHA/Coll as a substitute can successfully, aid in the process in the process of regenerative osteogenesis. In addition, there are multiple other studies which are currently investigating the use of ceramic based bone graft substitutes as an alternative for spinal treatment.

### **3.39 Regeneration of Bone Using Bone Graft Containing Collagen/ B-Tricalcium Phosphate**

Autologous bone transplantation is considered as the benchmark when it comes to bone repair. However due to the rise in complications, bone tissue engineering is viewed as an alternative approach. It uses a combination of different osteogenic cells, biocompatible scaffolding and growth promoting factors. The components involved in production of bone grafts should satisfy the following criteria—osteoinductive, osteoconductive and biocompatible. Type I collagen (Col-I) serves as a suitable candidate for bone tissue engineering due to its osteoconductive properties. The amalgamation of type-I collagen and calcium phosphate ceramics will serve as an excellent substitute for promoting bone regeneration. The  $\beta$ -tricalcium phosphate ( $\beta$ -TCP) is widely used as a filler in bone defects, due to its reabsorption and osteoconductive property. In addition, during the bone remodelling process it undergoes a slower degeneration and favours the osteogenesis process.

For the experimental study, a total of 12 white rabbits were taken and divided into three groups, A, B and C respectively and were placed under regulated environmental conditions. To treat the bone defect in the calvaria, a small incision was made followed by which each group of rabbit were subjected to different mode of treatment. In case of group-A and B the defect was filled with COL/  $\beta$ -TCP scaffold and COL scaffold respectively. While for group C, the defect was not remedied since it served as a negative control. Further histological examination was conducted using alizarin red dye, to observe the process of mineralization.

Based on the findings, it was concluded that the COL/  $\beta$ -TCP scaffold is better suited to repair and regenerate bone defects. Furthermore, COL/  $\beta$ -TCP scaffold can be employed more widely in future clinical cases because of the strong resemblance between the bio-ceramic component and mineral composition of the bone. After 8 weeks of implantation, it was observed that the group treated with COL/  $\beta$ -TCP scaffold was able to heal the bone defect much better than the COL scaffold. This is mainly because of the addition of  $\beta$ -TCP, which provides calcium and phosphate ions responsible for developing an environment which encourages the process of bone repair and regeneration. In case of COL/  $\beta$ -TCP scaffold, Masson's trichrome staining confirmed, that after 4 and 8 weeks the formation of immature bone and new bone generation was initiated respectively.

### **3.40 Cohort Study to Assess the Periprosthetic Bone Mineral Density and Bone Turnover after Osseo Integrated Surgery**

Osseo integration implantation is mainly performed on patients who have underwent transtibial and trans femoral amputations that is amputation below the knee and above the knee respectively. The Osseo integrated surgery enables the attachment of a rigid clinically approved alloplastic material to the bone. Thereby attenuating the pain endured by the patient. In this surgery, most commonly a titanium fixture is Osseo integrated with the residual femoral bone. Further an abutment is projecting through the skin, which aids in locking the prosthetic leg. The main aim of this study is to scrutinize the preoperative Bone marrow density (BMD) and the systematic bone turnover in patients with Trans femoral amputation. About 19 patients had undergone Trans femoral

amputations, forms the test group. While the patients in the control group were mainly selected from AutoRSA database. All the patients were examined preoperatively before knee or hip arthroplasty. In addition, blood samples were collected for identification of bone turnover markers such as C-telopeptide and N-terminal propeptide of type-I collagen (CTX and NTX), parathyroid hormones (PTH) and vitamin D. The findings of this study provide an overview of the mechanisms leading to septic and aseptic ablation of implants. The results indicated a significant decline of 15% and 35% in the mean BMD values for both the groups. During the 30-month investigation, around 4 and 3 patients underwent complete removal of the Osseo-integrated implant and the abutment due to development of severe infection and spiralling pain respectively. The concentration for PTH and CTX were found to be higher in case of patients who have undergone surgery for removal of prosthetic implants. Patients with trans femoral amputation had a comparatively lower BMD in the proximal femur on the amputated side than the control group on the intact side. In addition, degeneration of type-I collagen will result in release of CTX and NTX. CTX, functions as a surrogate marker used to evaluate metabolic product.

## **4. CONCLUSION**

This research review's purpose is to help the reader understand different aspects posed by the research on the therapeutic activity of collagen and rosehip extracts. This is significant because it gives insights about usage of collagen with rosehip extracts. There has been much research and discussion conducted on these opinions of usage and activity of both. Most of the research found, shows therapeutic activity of collagen and rosehip extracts in ortho related problems and ortho post-surgery. More research and testing is required to gain a better understanding of the therapeutic activity of collagen with rosehip extracts

## **AVAILABILITY OF DATA AND MATERIALS**

The author confirms that the data supporting the findings of this research are available within the article.

## **ACKNOWLEDGEMENT**

We would like to thank our supervisor/guide Bharat Kwatra, from Invenzion Labs Inc. whose

expertise was invaluable in formulating the research questions, methodology and drawing conclusions. His insightful feedback and guidance pushed us to sharpen our thinking and brought our work to a higher level.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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