

## EVALUATION OF THE EFFICACY AND SAFETY OF CAPSULE BONTON IN OSTEOPOROSIS

### AN OPEN CLINICAL TRIAL



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### ABSTRACT

Osteoporosis is a generic term referring to a state of decreased mass per unit volume (density) of normally mineralized bone. It is the most common skeletal disorder in the world and is second only to arthritis as a leading cause of musculoskeletal morbidity in the elderly. The most prevalent complications of osteoporosis are compression fractures of the vertebral bodies and fractures of the ribs, proximal femur, humerus and distal radius all occurring with minimal trauma!

The most common cause of osteoporosis is involutinal bone loss. Every woman in the perimenopausal age group is at risk, and more than 15 million women in America have symptomatic disease. Age related bone loss begins at about 40. Women lose about 35% to 40% of their cortical bone and 55% to 60% of their trabecular bone, whereas men lose about two-thirds of these amounts throughout life. The present study was conducted to evaluate clinical efficacy and short-term safety of Capsule Bonton in patients suffering from osteoporosis. This study was an open clinical trial undertaken in 30 patients of osteoporosis of either sex, in age cadre of >40 years. Ambulatory patients of age related and postmenopausal osteoporosis with subjective (low backache) and for objective positive findings were included in the study. Patients with established hypertension, renal/hepatic/cardiac failure, on long term steroid treatment, uncontrolled diabetes mellitus, autoimmune genetic disorder were excluded from the study. Patients with secondary osteoporosis were also excluded from the study. Proper recording of signs and symptoms with systemic and back and spine examination; thorough

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biochemical examination; plain radiographs of LS spine and Quantitative CT scanning of lumbar spine were done at baseline. The patients were evaluated clinically every fortnightly for 3 months and thoroughly analysed at the end of 3 months. Repeat plain radiographs of LS spine, Quantitative CT Scanning of lumbar spine and biochemical evaluation was done at the end of 3 months. A proper scoring system was used for subjective analysis. Efficacy was assessed by the decrease in total sign and symptom score at the end of 3 months and by improvement in radiological picture/ Quantitative CT Scan at the end of 3 months. Safety was assessed by incidence of adverse effects, and laboratory evaluation. Significant symptomatic improvement was seen in all patients by the end of the therapy. There was no significant alteration in hematological parameters, post therapy. 59.3% improvement in intensity, 74.68% in pain, 97% in Tenderness, 58.8% in Paraspinal stiffness / spasm and 67.74% improvement in average score has been reported in clinical symptoms. Radiological examination done at 3 months did not show any deterioration when compared to the pre therapy images. The trabecular bone measurement, done by Quantitative CT Scanning, showed significant improvement in 24 cases; while in rest of the 6 cases, there was no change/minor decrease at the end of 3 months. There was no incidence of any untoward side effects, during the entire trial. This study thus indicated that Capsule Bonton was very safe and effective for long term use in the management of established osteoporosis.

### INTRODUCTION

Osteoporosis is a common disorder of bone, particularly occurring in the elderly patients. It is second only to arthritis, as a leading cause of musculoskeletal morbidity in the elderly. Osteoporosis is defined as a disease characterized by low bone mass, micro architectural deterioration of bone tissue leading to enhanced bone fragility, and a consequent increase in the fracture risk.

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### Major risk factors of osteoporosis are

1. Age (advanced)
2. Sex (female)
3. Race (Caucasian and Asians)
4. Habitus (Petit or thin)
5. Menopause (premature, surgically induced)
6. Family History (positive)
7. Life style (cigarette smoking, alcohol abuse, limited physical Exercise, inadequate calcium intake)

Involitional osteoporosis is the most common form and is divided into two major clinical syndromes.

Type I: Postmenopausal osteoporosis (increased osteoclast activity, Increased bone resorption, mainly trabecular bone loss)

Type II: Age related osteoporosis (decreased osteoblast activity Decreased formation, cortical and trabecular bone loss)

### Other less common causes of secondary osteoporosis include

1. Endocrine disease e.g. Hyperthyroidism, Diabetes Mellitus, Hyperparathyroidism etc
2. Gastrointestinal disease e.g. malabsorption syndrome, severe Malnutrition etc
3. Bone marrow disorders
4. Connective tissue disorders
5. Miscellaneous e.g. immobilization, Rheumatoid arthritis etc.

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Patients with osteoporosis may be completely asymptomatic. Alternatively a history of thoraco-lumbar backache whilst at rest or during routine daily activity may be the earliest symptom. Pain is usually of sudden onset, increases with sitting, standing, sneezing, coughing and is relieved by rest. Incremental loss of height and mid thoracic kyphosis may also be evident (due to wedging of vertebral bodies). Patients may also present with appendicular fractures (especially proximal femur, humerus, and distal radius).

The predominant feature of age related and post menopausal osteoporosis is lack of abnormal hematological and biochemical findings. Classically CBC with ESR, serum calcium, serum albumin, serum phosphorus, serum alkaline phosphatase, blood urea, serum creatinine are normal. Elevation of serum alkaline phosphatase may occur following fractures.

Plain radiographs of thoracic and lumbar spine may reveal accentuation of end plate shadows, diffuse demineralization and compression fractures. Measurement of bone density has become an essential procedure in the diagnosis and treatment of osteoporosis. In addition, serial measurements are also useful to assess the response to treatment. The three widely available methods for the same are

1. single photon absorptiometry
2. Dual photo absorptiometry
3. Quantitative computed tomography

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The management of osteoporosis has two facets:

### 1. TREATMENT OF ACUTE SYMPTOMS

- ❖ Adequate rest
- ❖ Analgesics and muscle relaxants
- ❖ Increased water intake
- ❖ Deep breathing during bed rest
- ❖ Hot water fomentation
- ❖ Low heeled, soft sole shoes
- ❖ Proper orthotic devices as required

### 2. MAINTENANCE OF SKELETAL MASS

- ❖ Sufficient weight bearing activities
- ❖ Avoidance of risk factors (smoking, alcohol, immobilization)
- ❖ High calcium diet
- ❖ Adequate lifelong calcium and Vit D intake
- ❖ Estrogen supplementation at menopause
- ❖ Newer antiresorptive drugs
- ❖ Injectable / intranasal calcitonin
- ❖ Oral bisphosphonates

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Bonton capsule is an ayurvedic poly herbal preparation containing extract derived from *cissus quadrangularis*, *terminalia arjuna*, *litsea chinensis*, *abha guggal*, *laxadi guggal*, *kukudantwak bhasma* and *muktashakti bhasma*. It is known to provide natural calcium, enhance fracture healing and facilitates osteogenesis.

The present study was conducted to evaluate efficacy and safety of Bonton capsule in cases of symptomatic age related and postmenopausal osteoporosis.

### MATERIALS AND METHODS

**AIM OF STUDY:** To evaluate the efficacy and safety of Bonton capsule in cases of symptomatic age related and postmenopausal osteoporosis

**STUDY DESIGN:** The study was an open clinical trial (post marketing surveillance) conducted in the department of orthopedics, Medical college, Baroda over the period of 6 months. A written informed consent was obtained from all the patients. Total 38 patients were incorporated out of which 30 continued till end of the study. Test medicine i.e. Bonton Capsules (Vasu Pharma) was given 2 capsules B.D. for 3 month.

**STUDY POPULATION:** Thirty patients of either sex in the age cadre of > 40 years, with symptomatic osteoporosis (low backache) that attended the department of orthopedics, SSGH, Baroda in May 2006, were enrolled in the study. They were put on Capsule Bonton B.I.D for three months.

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**INCLUSION CRITERIA:** Ambulatory of both sex in the age cadre of > 40 years, with age related / postmenopausal osteoporosis were included in the study. All patients had complaint of low backache for at least 2 months prior to the study. These patients had radiological evidence of accentuation of end plate shadows and diffuse demineralization.

**EXCLUSION CRITERIA:** Patients with established hypertension, renal/hepatic/cardiac failure, on long-term steroid treatment, uncontrolled diabetes mellitus, genetic or autoimmune disorders were excluded from the study. All the cases of secondary osteoporosis were also excluded from the study.

**METHODOLOGY:** Selected patients underwent a complete physical examination before the trial. All signs and symptoms with regard to severity and duration were recorded before commencing treatment. A thorough systemic and back and spine examination was also performed.

Biochemical evaluation in the form of CBC with ESR, serum calcium, serum phosphorous, serum albumin, RA factor, serum alkaline phosphatase, blood urea, serum creatinine, BUN, thyroid profile, LFT and serum parathyroid hormone was done in all cases before initiating therapy.

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A baseline plain radiograph LS spine AP and lateral views and quantitative CT scanning of lumbar spine was also performed.

**Table - 1**

Total Enrolment	38
Completed Patients	30
Average Age	57±15
Male: Female	50: 50
> 60 Years	11
< 50 Years	5

**FOLLOW UP AND ASSESSMENT:** Subjective and objective evaluation was carried out every fortnightly for three months, with a final follow up at the end of three months. A proper scoring system was designed to evaluate subjective and objective findings, which was compared pre and post therapy.

A repeat biochemical evaluation (CBC, blood urea, SGOT, Serum calcium); Plain radiographs LS spine and Quantitative CT Scan were performed at the end of three months.

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**Table - 2**

Test Name	B.T.	3 Months
Average Hb g/dl	13.21	13.27
Average Blood Urea mg/dl	19.63	20.50
<b>Average SGOT IU/L</b>	<b>25.33</b>	<b>25.63</b>
Average Serum Calcium - Total mg/dl	8.93	9.07

**PRIMARY OUTCOME MEASURES:** Efficacy was assessed by a decrease in the total clinical score at the end of three months. The clinical score was based on the intensity of backache, degree of pain, lower back tenderness and Para spinal stiffness and spasm. It was also assessed by any improvement in radiological picture / trabecular bone mass measurement by QCT.

Intensity of backache	Mild	1
	Moderate	2
	Severe	3
Pain on	More than routine work	0
	Routine work	1
	Less than routine work	2
	At rest	3
Para spinal tenderness	Absent	0
	Present	1
Para spinal stiffness and spasm	Mild	1
	Moderate	2
	Severe	3

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Maximum pre-therapy score 10

### Results:

All patients were in the age cadre of  $\geq 40$  years. The male to female ratio was equal. Before initiation of therapy, all patients had moderate to severe backache, pain on rest or on less than routine work, Paraspinal tenderness and moderate to severe Paraspinal stiffness and spasm.

Following clinical parameters were tracked during the study.

1. Over all symptom intensity
2. Pain
3. Tenderness
4. Paraspinal Stiffness & Spasm
5. Average symptom score

### Intensity:

Table –3

Intensity	B.T.	15 Days	1 Month	2 Months	3 Months
Mean : B.T.	2.47	2.47	2.47	2.47	2.47
: A.T.		1.97	1.50	1.10	1.03
% Improvement		20.24	39.27	55.46	59.30
S D ( $\pm$ )		0.18	0.51	0.31	0.18
S E ( $\pm$ )		0.03	0.09	0.06	0.03
' t '		15.22	10.42	24.20	43.82

In the first fortnight patient reported average 20.24% improvement, which was 59.3% at the last intervention i.e. after 3 months. Not only the average intensity is improving progressively in all the interventions, it was reported improved in most patients.

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### Pain:

Table – 4

Pain	B.T.	15 Days	1 Month	2 Months	3 Months
Mean : B.T.	2.37	2.37	2.37	2.37	2.37
: A.T.		1.63	1.30	0.70	0.60
% Improvement		31.22	45.15	70.46	74.68
S D (±)		0.49	0.53	0.47	0.50
S E (±)		0.09	0.10	0.09	0.09
' t '		8.27	11.06	19.46	19.39

The improvement in pain was almost instant. Average improvement in 15 days was 31.22%, which progress to 74.68% improvement by the end of 3 months. The improvement was so dramatic that it was almost gratifying in most cases except 2 patients i.e. No.1 & 28, where in the improvement was only minor till end of first month.

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### Tenderness:

Table - 5

<b>Tenderness</b>	<b>B.T.</b>	<b>15 Days</b>	<b>1 Month</b>	<b>2 Months</b>	<b>3 Months</b>
Mean : B.T.	1.00	1.00	1.00	1.00	1.00
: A.T.		0.97	0.63	0.07	0.03
% Improvement		3.00	37.00	93.00	97.00
S D (±)		0.18	0.49	0.25	0.18
S E (±)		0.03	0.09	0.05	0.03
' t '		0.91	4.14	20.38	29.52

At the first intervention, improvement was only minor i.e. 3%, whereas visible difference started from the first month i.e. 37% improvement, 93% improvement at second month and 97% improvement at the end of third month. The first month improvement is not statistically significant but the second and third month improvement is statistical significant ( $p < 0.001$ ).

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### Paraspinal Stiffness & Spasm:

Table - 6

<b>Paraspinal Stiffness &amp; Spasm</b>	<b>B.T.</b>	<b>15 Days</b>	<b>1 Month</b>	<b>2 Months</b>	<b>3 Months</b>
Mean : B.T.	2.50	2.50	2.50	2.50	2.50
: A.T.		2.00	1.63	1.07	1.03
% Improvement		20.00	34.80	57.20	58.80
S D (±)		0.00	0.49	0.25	0.18
S E (±)		0.00	0.09	0.05	0.03
' t '		-----	9.72	31.33	44.73

Average improvement at 15days was 20%, after one month 34.8%, after two months 57.2% and 58.8% at the end of third month. The difference between second and third month is not great. Nevertheless, 58.8% improvement in Paraspinal Stiffness & Spasm is a great relief to the patient.

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#### Average score:

Table - 7

Average Score	B.T.	3 Months
Mean : Pre-therapy	8.37	8.37
: Post-therapy		2.70
% Improvement		67.74
S D ( $\pm$ )		0.65
S E ( $\pm$ )		0.12
' t '		47.78

The mean improvement of all the clinical symptoms was 67.74%.

It can be safely concluded that the product under investigations i.e. Bonton Capsules is effective in symptomatic relief. The improvement can be visible from first month onward and continues to improve with continuation of the therapy.

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### **Bone marrow measurement (Quantitative CT Scanning)**

Table -8

<b>Trabec.</b>	<b>B.T.</b>	<b>3 Months</b>
Mean: Pre-therapy	123.46	130.39
: Post-therapy		130.39
% Improvement		5.61
S D (±)		32.35
S E (±)		6.60
' t '		1.049

There was a significant increase in the trabecular bone mass (as measured by QCT of lumber spine) in 24 patients at the end of three months (of which 38.8% were females). The remaining patients had minor decrease and no significant alteration in trabecular bone mass at the end of the study. While the average improvement of all the patients comes to 5.61% in QCT, the same certainly indicates a positive change, which if improved upon continuation of treatment with Bonton Capsules can be of great relief to the elderly patients. It is recommended to continue the study for another nine months so as to measure the changes in bone density over the period considering the chronic nature of the condition.

### **ADVERSE DRUG REACTIONS:**

No untoward side effects were reported during the entire period of trial in all the 30 patients.

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*DISCUSSION:* Osteoporosis is most common skeletal disorder in the world and is second only to arthritis as a leading cause of musculoskeletal morbidity in the elderly. If Hypertension is the silent killer, then osteoporosis is the silent thief. It insidiously robs the skeleton of its bank resources- often for decades- until the bone is so weak that it cannot withstand normal stress. Areas of high trabecular bone remodeling, such as the thoracic and lumbar vertebral bodies, ribs, proximal femur, humerus, and distal radius, sustain most of the damage. It is necessary to encourage the reduction of avoidable risk factors and continue to educate women about the potential benefits ( and risks) perimenopausal estrogen use. The medical community has to continue its search for better, safer, less expensive and more convenient antiresorptive agents and regimens.

Herbal formulations have been proven to be as effective and safer alternatives to conventional drugs. Bonton capsule is an ayurvedic poly herbal preparation containing extract derived from cissus quadrangularis, terminalia arjuna, litsea chinensis, abha guggal, laxadi guggal, kukudantwak bhasma and muktashakti bhasma. It is known to provide natural calcium, enhance fracture healing and facilitate osteogenesis. Cissus Quadrangularis contains high amount Vit C, Carotene A, anabolic steroidal substances and calcium. It has been known to possess significant cardio tonic, androgenic, analgesic and osteogenic properties.

In this study, there was a significant symptomatic relief at the end of the therapy. An overall improvement in the quality of life was evident. There were no significant alterations in hematological/ biochemical parameters at the end of study. There was no radiological deterioration at the end of three months, as compared to the pre therapy images. There was a significant improvement in the trabecular bone mass (in 18 out of 30 patients) at the end of three months. There was no evidence of any ADR reported during the entire duration of the clinical trial.

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#### CONCLUSION:

Osteoporosis remains the most common skeletal disorder in the world and is the common cause of morbidity and compromise in the quality of life.

Current osteoporotic drugs have their own limitations regarding their host ADRs and are therefore of questionable advocacy for long-term use. Furthermore the chronic nature of osteoporotic process itself demands a long-term therapy for years together.

This study indicate that the Bonton Capsule provides an effective and safer alternative for long term management since it improves in symptoms score at the same time positive changes are observed radiographically.

During the study, no incidences of untoward effects were reported.

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