



1. Introduction

ThankGod™ (Euphorbia prostrata dry extract) is a completely safe and effective **herbal drug** that helps in **effective relief from various signs and symptoms of haemorrhoids** including bleeding, anal discomfort, anal itching, pain at prolapse and proctitis in first and second degree\degree haemorrhoids. It has also been shown to be quite effective in terms of non-recurrence of bleeding.

2. Medical Need

Haemorrhoids are very common in both men and women. About half of the population has haemorrhoids by the age of 50. Haemorrhoids are also common among pregnant women. Haemorrhoids is characterized by dilated sub mucosal veins which may thrombose and rupture with haematoma formation. External haemorrhoids form beyond the intersphincteric groove to produce an "acute pile" at the anal verge. Chronic constipation, chronic diarrhoea, pregnancy, and portal hypertension enhance haemorrhoid formation. Haemorrhoids can itch and bleed (usually bright red blood, during defecation).

3. Formulation

The anti-haemorrhoidal drug (**ThankGod™**) developed by Panacea Biotec has a multimodal approach towards haemorrhoids treatment. It helps in the reduction of inflammation and pain, haemostasis, wound healing and protection of vascular walls.

The **principle active constituents** of **ThankGod™** (Euphorbia prostrata dry extract) include flavonoids like apigenin, luteolin, quercetin (and their glucosides), phenolic acids like ellagic acid, gallic acid and tannins. All these constituents have been shown to affect the function of enzyme systems critically involved in the generation of inflammatory process like hyaluronidase, protein kinase C, 5 –lipoxigenase, cyclooxygenase etc. They also decrease leukocyte infiltration in the inflammatory tissue and inhibit platelet

adhesion, aggregation and secretion. The phenolic acids activate intrinsic blood coagulation by activation of Hageman factor and cause a state of hypercoagulability.

3.1 Mechanism of action

Ability of the flavonoids to increase capillary resistance and to inhibit capillary permeability has been their oldest recognized pharmacological activity. The following mechanisms of this activity have been proposed:

- ▪ Chelate formation with metals thereby inhibiting oxidation of ascorbic acid.
- ▪ Protection of epinephrine by inhibition of O-methyl transferase that maintains the capillary tone
- ▪ Stimulation of pituitary-adrenal axis
- ▪ Inhibition of blood cell aggregation

For preparation of **ThankGod™** capsules, the semisolid extract has been adsorbed onto rapidly gastro soluble inert ingredients, to prepare a free flowing dry powder. This powder has been filled in hard gelatin capsules. After administration, the capsule contents dissolve readily, making the extract bioavailable.

4. Preclinical experience

- ▪ The **ThankGod™** formulation was evaluated for analgesic activity using acetic acid writhing assay in mice and for anti-inflammatory activity using carrageenan induced rat paw oedema.
- ▪ **ThankGod™** produced significant antinociceptive effect 90 minuter after its oral administration. The effect lasted up to 2 hours post administration. **ThankGod™** produced dose dependent antinociceptive effect.
- ▪ **ThankGod™** dose dependently and significantly decreased the carrageenan induced increase in paw volume as compared to control rats. The onset of anti-inflammatory effect was quick and lasted upto 4 hours of inflammation (post carrageenan).

Table 1: Percentage inhibition of Rat paw oedema at 90 and 120 minutes post administration of ThankGod™

No.	Treatment	90min	120 min
1.	ThankGod™ (5mg/kg)	25.82	23.60
2.	ThankGod™ (10mg/kg)	44.58	40.55
3.	ThankGod™ (20 mg/kg)	74.67	56.77
4.	ThankGod™ (40mg/kg)	71.00	64.03

Conclusion

ThankGod™ formulation was reported to have a significant analgesic and anti-inflammatory activity.

- **Toxicity studies**

The acute and sub acute toxicological studies of compound **ThankGod™** were conducted in albino rats and guinea pigs. In acute toxicity studies, no mortality was observed on p.o. administration of drug upto 5gm/kg dose. The sub-acute toxicity studies were conducted in rats and guinea pigs by using their 1/5, 1/10 and 1/20 of LD-50 doses achieved by i.p. route. The drug was administered p.o. daily for 14 days. The test groups of animals did not show any signs of toxicity and biochemical, hematological, parameters remained unaltered when compared with control groups. The drug was relatively safe; rats and guinea pigs were able to tolerate the drug upto 428mg/kg and 300mg/kg p.o. respectively on subacute administration for 14 days.

5. Clinical Experience

5.1 Study I

(Conducted in New Delhi, India) A 125 volunteer double-blind, placebo controlled, comparative, prospective, randomized clinical evaluation of two doses of standardized *Euphorbia prostrata* extract in capsule formulation to determine the optimal dose, efficacy, safety and patient tolerability in acute haemorrhoidal attacks.

Observations

- ▪ At day 5, complete recovery from anal discomfort and proctorrhagia was found to be the highest in the 100mg dosage (TDB) group
- ▪ The degree of overall improvement and reduction in symptoms of acute haemorrhoidal attacks was the highest in the TDB group on both assessment days (Day 5 & Day 10)
- ▪ Clinically the TDB group showed better decrease in bleeding episodes at both Day 5 and Day 10
- ▪ At 3 months follow up, both treatment groups i.e the 50mg dosage (TDA) group and the 100 mg dosage (TDB) group were found to be quite effective in terms of non-occurrence of bleeding
- ▪ In degree II haemorrhoids of all the treatment groups, TDB showed better results in anal discomfort and proctitis on Day 5
- ▪ In proctorrhagia, anal discharge and pain at prolapse both TDA & TDB were comparable but better than TDC (placebo) clinically
- ▪ At Day 5, TDB proved to be a better drug in bringing about complete disappearance of signs and symptoms of acute haemorrhoidal attacks
- ▪ The use of rescue medication in Degree I and Degree II haemorrhoids was seen in lesser number of patients in TDB group at the end of the therapy (Day 10)

Conclusions

- ▪ Both TDA (50mg) and TDB (100mg) were found to be highly effective in management of I & II degree of haemorrhoids. TDB (100mg) capsule once a day for 10 days might prove to be a more useful therapy for the treatments of I & II degree

haemorrhoids in near future. In this study, flavonoids in two doses showed good efficacy in treatment of haemorrhoids.

5.2 Study II

Six hundred and sixty-nine (669) subjects were selected for an open labelled, non-comparative prospective observational study to assess the efficacy, safety and tolerability of 100 mg **ThankGod™** Relief Capsules and **ThankGod™** Anytime Cream (containing standardized extract of *Euphorbia prostrata*) in I and II degree haemorrhoidal disease.

Observations

- ▪ After ten days of therapy with **ThankGod™** Relief Capsules and **ThankGod™** Anytime Cream all the symptoms and clinical parameters related to the performance and efficacy were significantly recognized. It is evident from the table below that subject with symptoms and clinical signs of haemorrhoids showed significant improvement during the course of therapy
- ▪ The relief in all the symptom and signs of haemorrhoids is significantly higher after ten days of treatment as compared to five days of treatment.

Parameters	Study Population N =669			
	Presence of signs and symptoms			
	Before Treatment (Baseline)	Visit 1 (Day 5)	Visit 2 (Day 10)	
Proctorrhagia	616 (92.1 %)	421 (63.1 %)*	63 (9.5 %)*†	
Anal Discomfort and pain	615 (91.9 %)	353 (52.9 %)*	45 (6.8 %)*†	
Anal Discharge	254 (38.0 %)	97 (14.5 %)*	17 (2.6 %)*†	
Proctitis (Itching)	477 (71.3 %)	221 (33.1 %)*	43 (6.5 %)*†	
Proctitis (Burning)	474 (70.9 %)	217 (32.5 %)*	21 (3.2 %)*†	

Prolapse(protoscopy)	188 (28.2 %)	125 (18.7 %)*	82 (12.4 %)*†
Excoriation	425 (63.7 %)	260 (39.0 %)*	46 (6.9 %)*†
Congestion	582 (87.3 %)	337 (50.5 %)*	68 (10.3 %)*†
Swelling	509 (76.3 %)	289 (43.3 %)*	43 (6.5 %)*†
Bleeding with Exudation	538 (80.7 %)	342 (51.3 %)*	59 (8.9 %)*†

*Statistically Significant (compared to baseline)

† Statistically Significant (compared to Visit 1 (Day 5))

Conclusions

- ▪ The study results of this post marketing observational study has further consolidated the evidence in favor of excellent efficacy and safety of 100mg **ThankGod™** Relief Capsules and **ThankGod™** Anytime Cream in relieving the symptoms of grade I & II hemorrhoids. Significant improvement was observed in all the parameters (signs and symptoms of hemorrhoids) analyzed in this study. The products were found to be safe as the adverse events reported were infrequent and minor and there were no changes in the laboratory parameters before and after 10 days of treatment.

6. Patent Status

ThankGod™ is patented in all major countries across the globe including:

- ▪ United States : US 5858371
- ▪ Europe : EP 868914
- ▪ Australia : AU 698407

7. Development Status

- Commercialized in the Indian market
- CTD compilation under process for regulated markets

8. Product Presentation

ThankGod™

Euphorbia Prostrata

Extract Capsule*

Each tablet contains:

Euphorbia prostrata

Extract 100 mg



** based upon the stability data of ThankGod™ capsules & Tablets it was observed that the stability profile of the tablets was found to be better than capsules, hence finished dosage form has now been changed to tablets*

ThankGod™

Euphorbia Extract Cream

30gm

Each gram contains

Euphorbia Prostrata

Extract 10mg

Crean base

q.s.

