Efficacy, safety and tolerability of 4-n-butylresorcinol 0.3% cream in Indian patients with melasma

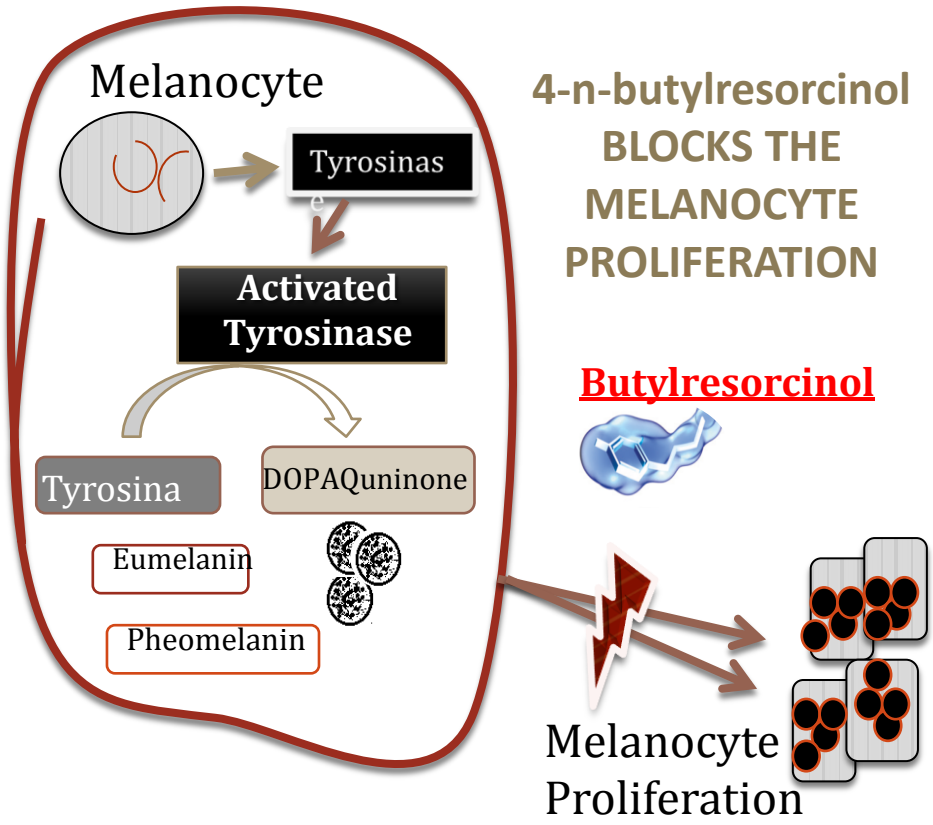
Introduction

- Melasma is the commonly reported pigmentary disorders in the Indian population.
- Numerous therapeutic modalities are available.
- However, very few have produced complete satisfactory response.
- 4-n-butylresorcinol 0.3% cream (***Onetone cream***) is recently introduced in India as a new hypopigmenting agent.

4-n-butylresorcinol

- 4-n-butylresorcinol, a resorcinol derivative inhibits both tyrosinase and TRP-1.

- Hypopigmenting action of 4-n-butylresorcinol was first reported in 1995, and subsequent *in vitro* and *in vivo* studies have documented its hypopigmenting efficacy.



4-n-butylresorcinol

- Numerous International clinical studies show 4-n-butylresorcinol to be a very potent, effective and safe in melasma.

- There is paucity of data on 4-n-butylresorcinol in Indian patients.

- Our study explores the efficacy, safety and tolerability of 4-n-butylresorcinol 0.3% cream in Indian patients with melasma.

ASSESSMENT OF EFFICACY, SAFETY AND TOLERABILITY OF 4-N- BUTYLRESORCINOL 0.3% CREAM IN INDIAN PATIENTS WITH MELASMA

FIRST INDIAN STUDY

Study Objective

- To investigate the hypopigmenting efficacy and safety of 4-n-butylresorcinol 0.3% cream for the treatment of melasma

Primary Outcome

- Evaluate efficacy of 4-n-butylresorcinol in reducing melasma

Secondary Outcome

- Evaluate safety and tolerability of 4-n-butylresorcinol

Dosing regimen

- A standard amount of cream with the fingertip-unit to be applied over the affected area(s) of the face, twice daily, for 8 weeks

- Subjects were not allowed to use any bleaching agents during the study.

- They were instructed to apply sunscreen. (SPF 30)

Study Design

- Multicentric Open label single arm study
- Study duration : 8 weeks
- The study was conducted according to the protocol and in accordance with ethical guidelines.
- All the subjects provided informed written consent prior to their participation
- The study conducted at each trial site after receiving approval from Institutional Ethics committee (IEC).
- The study registered in Clinical Trial Registry of India(CTRI). (CTRI Ref No. 2014/12/008073)

Study Centre -1

- **Dept. Dermatology, Dr. B.R.Ambedkar Medical College (BRAMC); Bangalore, India**

•Principal Investigator	➢ Dr. Madan Mohan Professor
•Co-Investigator	➢ Dr. Shilpa Shree Asst. Professor
•Scientific Advisor	➢ Dr. (Maj. Gen.) A K Jaiswal Professor & HOD

Study Centre - 2

- **Dept. Dermatology, Kempegowda Institute of Medical Sciences (KIMS); Bangalore, India**

•Principal Investigator	➢Dr. Adarsh Gowda Asst. Professor
•Scientific Advisor	➢Dr. Sharath Kumar BC Professor & HOD

Inclusion Criteria

- Subjects with melasma who are either treatment naive or were not on any treatment for at-least 6 months
- Subjects aged 18 and above years with melasma
- Subjects with Epidermal type of melasma
- Subjects with Fitzpatrick skin types III, IV and V
- Subjects willing to return for all clinic visits and complete all study-related procedures

Exclusion Criteria

- Subjects with dermal or any other type of melasma other than epidermal type
- Subjects who are either pregnant or breast feeding
- Subjects taking oral contraceptive pills
- Subjects with endocrinopathies
- Subjects on phototoxic drugs, anticonvulsant medications and the use of certain cosmetics which are known to cause hyper pigmentation
- Subjects taking any other form of alternative treatment like ayurvedic etc. for melasma
- Subjects known to have hypersensitivity to any of the ingredients of the formulation

Efficacy Evaluation

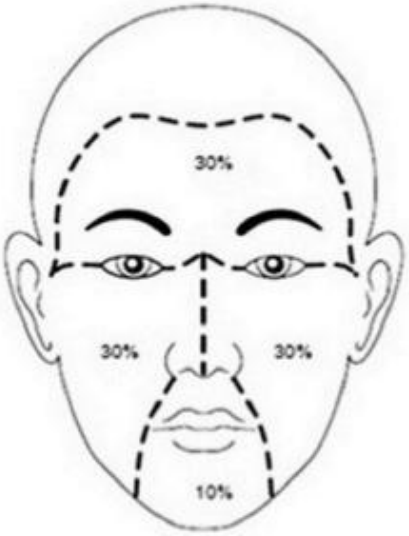
Decrease in Melasma evaluated through

- **MASI score** (Melasma Area and Severity Index)
- **Digital Photographs**

MASI SCORE

- The severity of the melasma in each of the four regions (forehead, right malar region, left malar region and chin) is assessed based on three variables: percentage of the total area involved (A), and darkness (D) and homogenicity (H)

Melasma Area and Severity Index MASI Score



The area (A) of melasma involvement is graded from 0 to 6:

- 0 = no involvement
- 1 = less than 10% involvement
- 2 = 10% to 29% involvement
- 3 = 30% to 49% involvement
- 4 = 50% to 69% involvement
- 5 = 70% to 89% involvement

The darkness of pigmentation (D) and homogeneity (H) graded from 0 to 4:

- 0 = absent
- 1 = slight
- 2 = mild
- 3= marked
- 4 = maximum

Safety Assessment

- Safety assessed through adverse events as mentioned by patient and evaluated by investigator.

Tolerability Assessment

Tolerability will be assessed by the investigator based on a 4-point scale as follows:

- **Excellent** = No adverse event reported
- **Good** = Mild adverse event(s) reported which subsided with or without medication and did not necessitate stoppage of study medication
- **Fair** = Moderate to severe adverse event(s) reported which subsided with or without medication and did not necessitate stoppage of study medication
- **Poor** = Severe or serious adverse event(s), which necessitated stoppage of study medication

Schedule of Visits

Activity	Day 0	Week 4	Week 8
Eligibility criteria	X	-	-
Informed consent	X	-	-
Photographic images	X	X	X
MASI score	X	X	X
Adverse effects	-	X	X
Concomitant medications	X	X	X

Results

Data from

Dermatology Department of

Dr. B. R. Ambedkar Medical College

(BRAMC)

Demographic data

- Total number of subjects enrolled : 27
- All the patients completed the study. No drop outs

Demographic Data	
➢ Male	2 (7.4%)
➢ Female	25 (92.6 %)
➢Mean Age	39.6 ± 8.5 years
➢ Occupation	Majority were housewives (48%).

Methodology

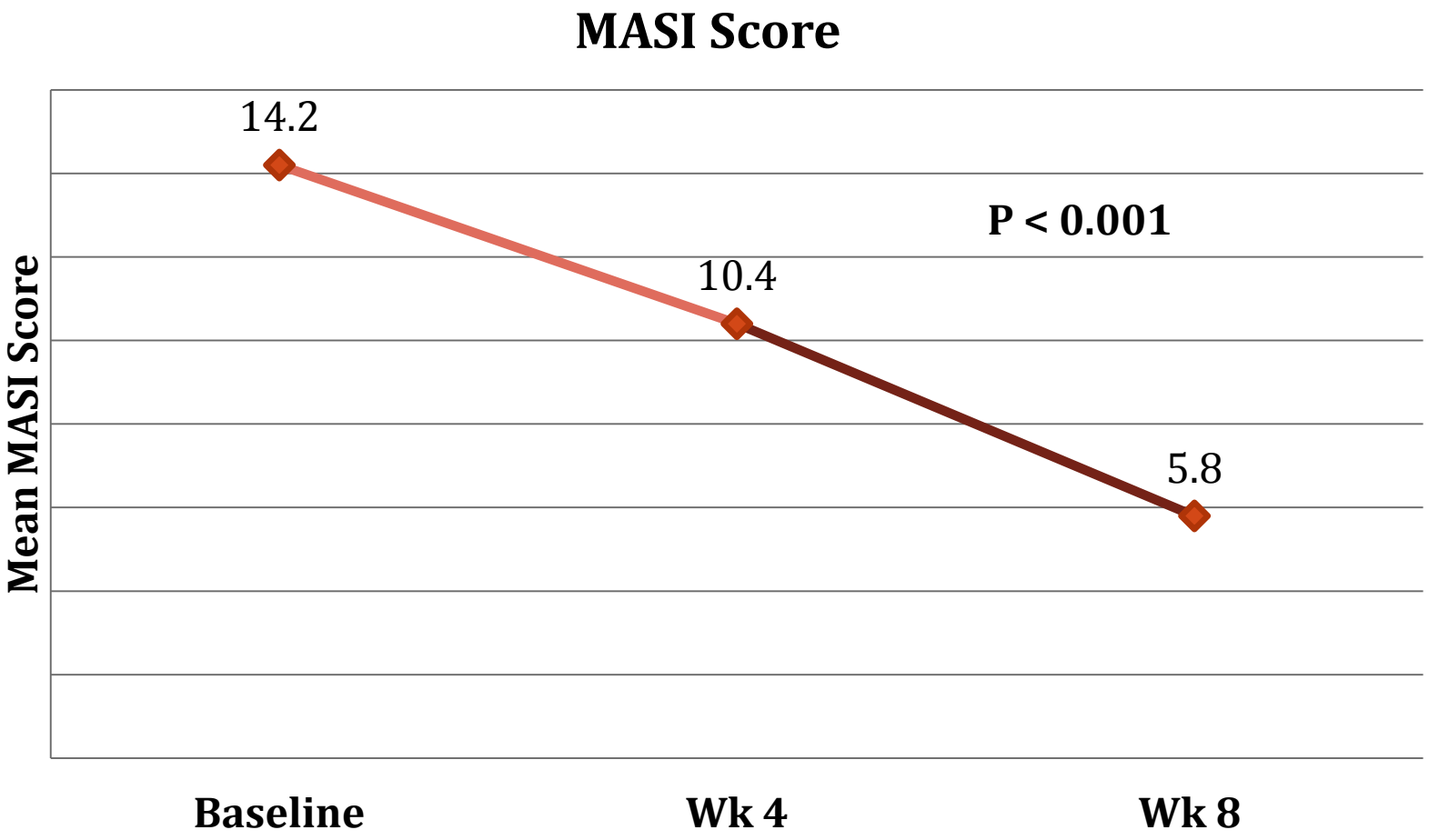
- The diagnosis of epidermal melasma was done by Wood's light lamp examination.

- All the recruited subjects visited the trial centers at baseline, week-4 and week-8.

Changes in MASI SCORE

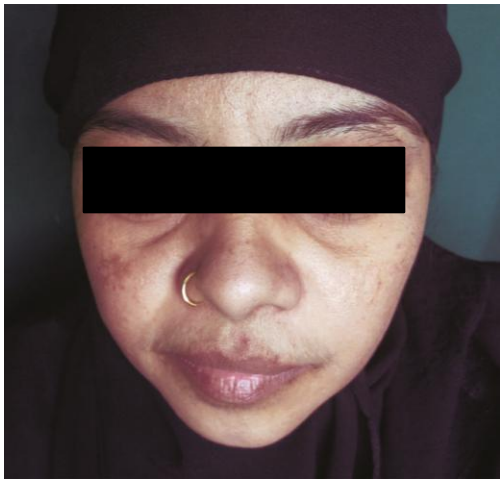
N= 25	Mean	S D
Baseline	14.2	±4.37
Week 4	10.4	±3.52
Week 8	5.8	±2.22

Changes in MASI SCORE

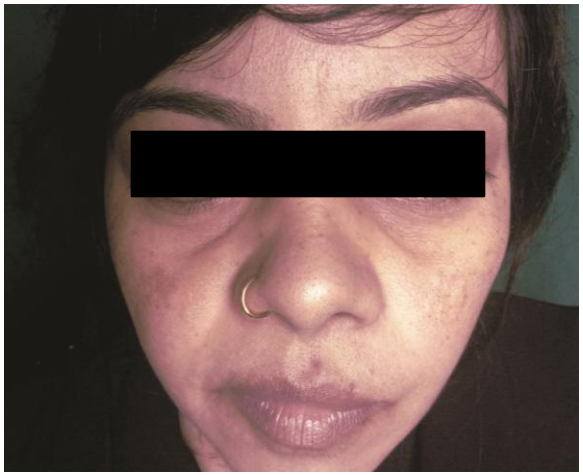


Gradual reduction in the MASI score over 8 week study period which was found to be statistically highly significant (P < 0.001)

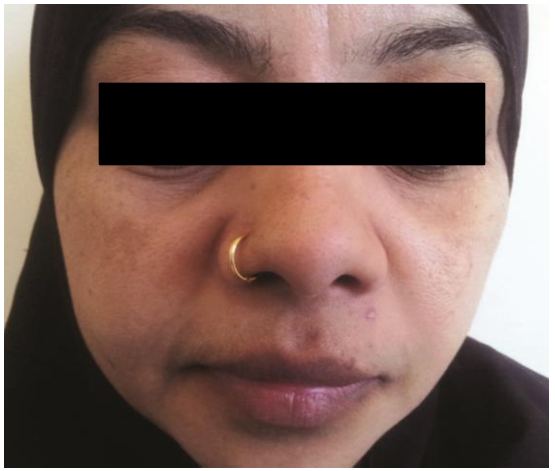
Photograph at baseline, after 4 weeks and after 8 weeks of therapy



Baseline

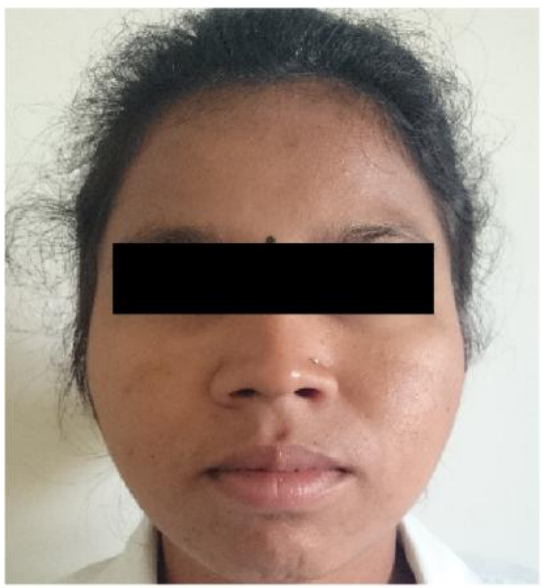


Week-4

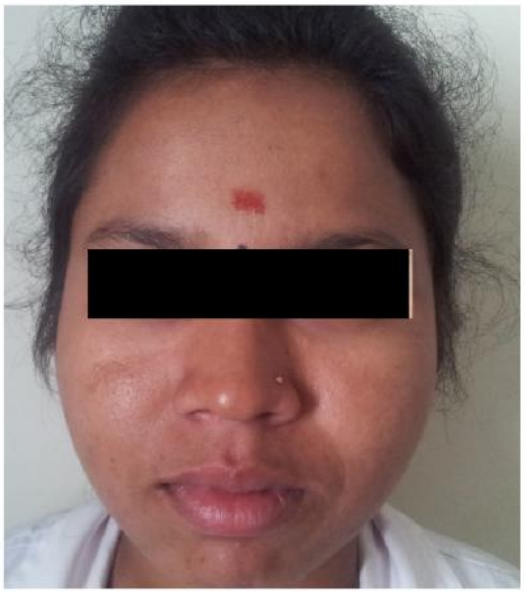


Week-8

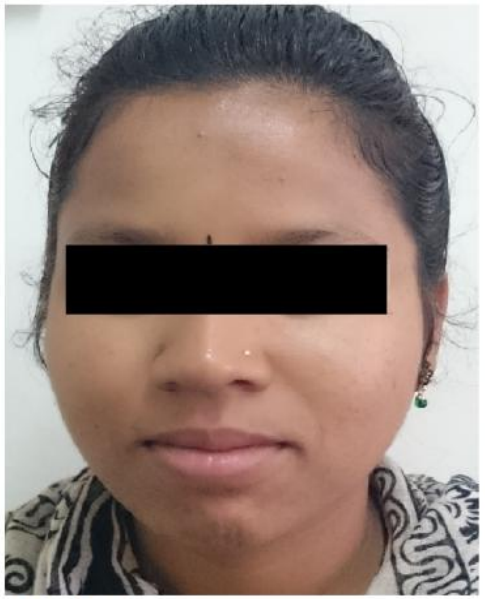
Photograph at baseline, after 4 weeks and after 8 weeks of therapy



Baseline



Week-4



Week-8

ADVERSE EVENTS

- All the patients well tolerated the treatment and there were no adverse event reported.

CONCLUSION

4-n-butylresorcinol 0.3% cream showed good efficacy and it was well tolerated when used for the treatment of melasma in Indian patients.

Thank you