# Herbal Nutritional Supplement
(CEREBRO-FLO: SR COMPOUND)
Based on
WHO Standards
Useful in
Treatment
of
# ALZHEIMER

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**Research Presentation**
**and**
**Collaboration Proposal**

**from**

**AAY Research Centre, India**
**and**
**KRASS Foundation, India**

Submitted By

**Dr. Sunil Kr. Gupta**
**Chief. Scientist**

**July 30, 2015**

# Contents

# 1 Objective

Objective of the submission is as follows

- Showcase of research work which has been done in field of Cerebral Perfusion and its application in treating Alzheimer.

- Partnership through Technical and Research Collaboration to apply the research for treating patients of Alzheimer.

# 2 Introduction

Alzheimer's disease (AD) is a senile dementia and is the most common form of dementia. This incurable, degenerative, and terminal disease was first described by German psychiatrist and neuropathologist Alois Alzheimer in 1906. Mostly it is prevalent after 60 years of age. Alzheimer's can also occur at early ages. In 2006 about 26.6 million cases were reported worldwide.

Approximately 10% of all persons over the age of 70 years have significant memory loss, and in more then half the cause is AD. It is estimated that the minimal annual total cost of caring for a single AD patient in an advanced stage of disease is >$50,000 (Harrison's Principals of internal medicine, 18$^{th}$ edition, 2011).

## 3 Pathophysiology

The aetiopathogenesis of Alzheimer's disease are not well understood. Pathologically it is associated with deposition of plaques and tangles in the brain. So far as the treatment is concerned it offers minimal symptomatic relief. Even progression of disease cannot be prevented.

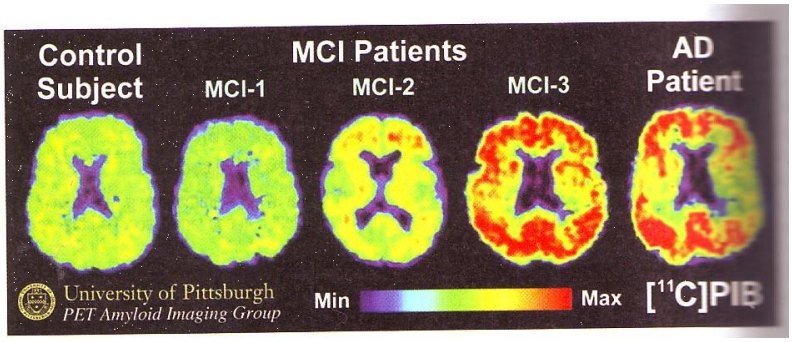
Till date many clinical studies have been conducted for a possible treatment of the disease, but no study have reported promising positive results. Even the preventive strategies suggested so far are of no help. Hence this disease is putting a pressure on social, psychological, physical, and economic elements of the caregiver's life. It is reported that AD is one of the most costly diseases to society in developed countries.

## 4 Biochemistry of AD

In Alzheimer's disease there is accumulation of abnormally folded A-beta and tau proteins in the brain. Beta-amyloid (A-beta or Aá) is a transmembrane protein that penetrates through the neuron's membrane. APP (amyloid precursor protein) is critical to neuron growth, survival and post-injury repair. In AD, this APP is divided into smaller fragments by enzymes through proteolysis. One of these fragments gives rise to fibrils of beta-amyloid, which form clumps that deposit outside neurons in dense formations known as senile plaques. In Alzheimer's disease, changes in tau protein lead to the disintegration of microtubules in brain cells. In AD, tau protein gets hyperphosphorylated and begins to pair with other threads, creating neurofibrillary tangles and disintegrating the neuron's transport system.

# 5 Cerebral Perfussion in AD

Apart from other Pathophysiological changes in neural tissue in cases of AD that there is definite increasing deficit in cerebral perfusion in cases of AD. Studies reported that SPECT studies on patients with AD showed Regional cerebral perfusion deficits. AD patients showed significant reductions in cortical/cerebellar activity ratio. Cortical perfusion is globally depressed with the largest reductions in frontal and posterior temporo-parietal cortices(1). Syed GM et al reported that even mildly demented patients, had parietal and temporal perfusion deficits, often unilateral. Moderate to severely demented patients had bilateral temporal and parietal perfusion deficits(2). Studies of Warkentin S et al reported that in AD a consistent finding in all subgroups was a significant deficit in temporoparietal blood flow of both hemispheres. Distinct group differences were seen in frontal, central and occipital areas with different combinations of involvement (3). Apart from this there many more studies reporting cerebral perfusion defects in AD.





1. Perani, D. ; Di Piero, V. ; Vallar, G. ; Cappa, S. ; Messa, C. ; Bottini, G. ; Berti, A. ; Passafiume, D. ; Scarlato, G. ; Gerundini, P. Technetium-99m HM-PAO-SPECT study of regional cerebral perfusion in early Alzheimer's disease. J. Nucl. Med.; (United States); Journal Volume: 29:9

2. Syed GM, Eagger S, O'Brien J, Barrett JJ, Levy R. Patterns of regional cerebral blood flow in Alzheimer's disease. Nucl Med Commun. 1992 Sep;13(9):656-63.

3. Warkentin S, Ohlsson M, Wollmer P, Edenbrandt L, Minthon L.Regional cerebral blood flow in Alzheimer's disease: classification and analysis of heterogeneity. Dement Geriatr Cogn Disord. 2004;17(3):207-14. Epub 2004 Jan 20.

# 6 Presentation of Problem in AD

The deficits in AZ may be the defects in form of:

- Language
- Memory
- Perception
- Emotional behavior or personality
- Cognitive skills (such as calculation, abstract thinking, or judgment)

The disease usually started with *Pre-dementia stag.* In this stage it present with forgetfulness. Mild cognitive impairment (MCI) are noted between normal forgetfulness due to aging, and the development of AD. It presents with difficulty in remembering recently learned facts and inability to acquire new information. It may take as long as 8 years between presentation of mild cognitive difficulties and fulfilling the clinical criteria for diagnosis of AD.

Other presentations may be in form of Subtle problems e.g. executing functions of attentiveness, planning, flexibility, and abstract thinking or impairments in sementic memory (memory of meanings, and concept relationships) in early stages of AD. Apathy can also be observed at this stage. This presentation of apathy remains the most persistent neurophychiatric symptom throughout the course of the disease.

Symptoms of MCI include:

- Forgetfulness of recent events or conversations
- Difficulty performing more than one task at a time
- Difficulty solving problems
- Taking longer to perform more difficult activities

The early symptoms of AD can include:

- Language problems, Misplacing items, Getting lost on familiar routes, Personality changes and loss of social skills, patient losses interest in things previously enjoyed, Difficulty in performing tasks that take some thought.

As the AD becomes worse:

- Symptoms are more obvious and interfere with your ability to take care of yourself. Such as forgetting details about current events, Change in sleep patterns, often waking up at night, Difficulty reading or writing, Poor judgment and loss of ability to recognize danger, Using the wrong word, mispronouncing words, speaking in confusing sentences, Withdrawing from social contact, Having hallucinations, delusions, depression, agitation and Difficulty in doing basic tasks.

People with severe AD can no longer:

- Understand language, Recognize family members, Perform basic activities of daily living, such as eating, dressing, and bathing

Other symptoms that may occur with AD:

- Incontinence
- Swallowing problems

The mean life expectancy after diagnosis is approximately seven years. Fewer than three percent of individuals live more than fourteen years after diagnosis.

# 7 Treatment

Since AD cannot be cured or prevented, **there is ray of hope that either the disease can be prevented or/and few presentations can be revert back by improving cerebral perfusion.**

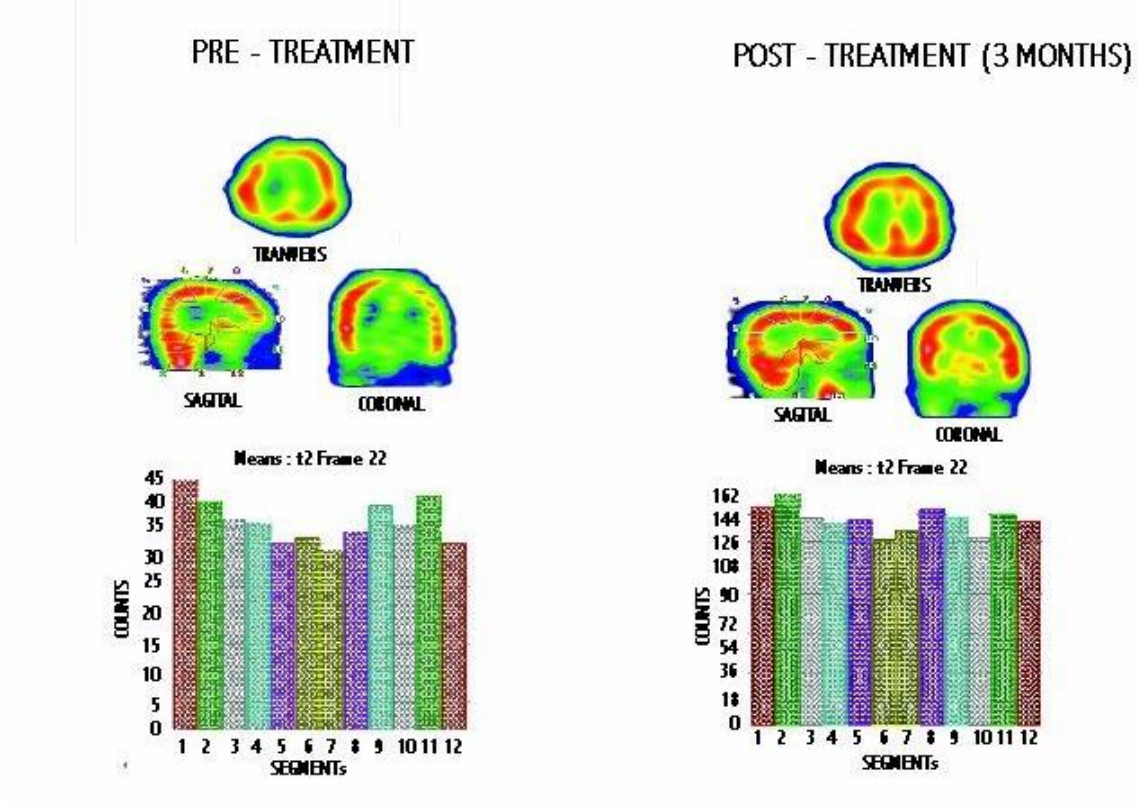
Few cases of AD indicated definitive clinical improvement in cases of AD when treated with herbal nutritional supplement. This herbal nutritional supplement documented the improvement in the cerebral perfusion when given to the patients with higher mental function disorder.

The reversal in clinical presentation is expected with the herbal nutritional supplement and the quantum of clinical improvement depends upon the level of improvement in cerebral perfusion and anatomical damage in the neural tissue.

The changes can be expected in 3-6 month of starting the supplement. Early cases may show clinical improvement as early as 3 weeks of starting the supplement.

## 8 Case studies showing improvement in Cerebral Perfusion

Here two case reports are given documenting improvement in cerebral perfusion after supplementing said herbal nutritional supplement.



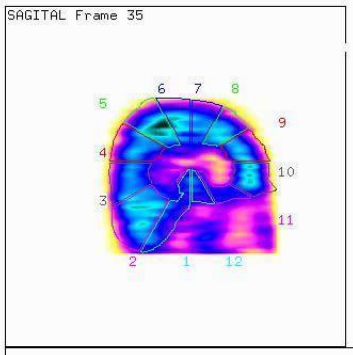
BRAIN SPECT-HMPAO

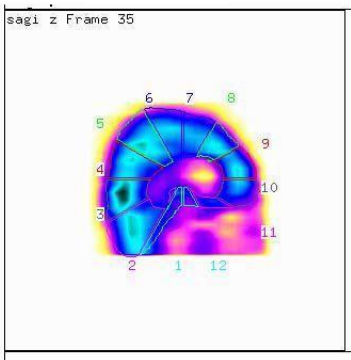
PRE-TREATMENT

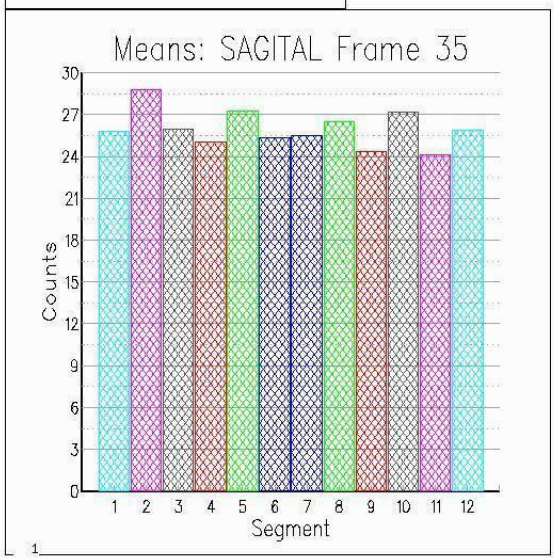
Sep 15, 1998 20:03

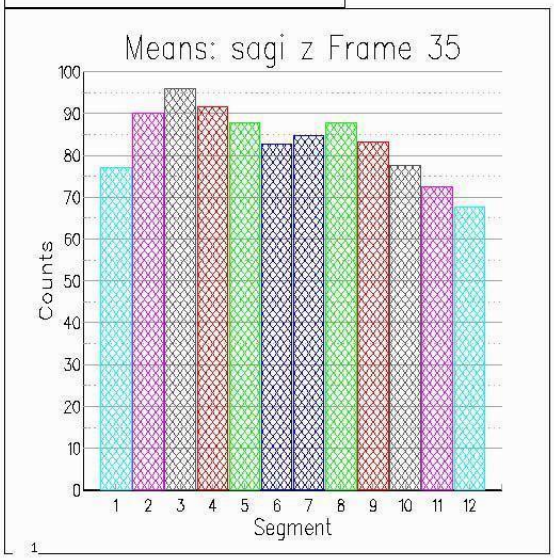
POST-TREATMENT

Jan 13, 1999



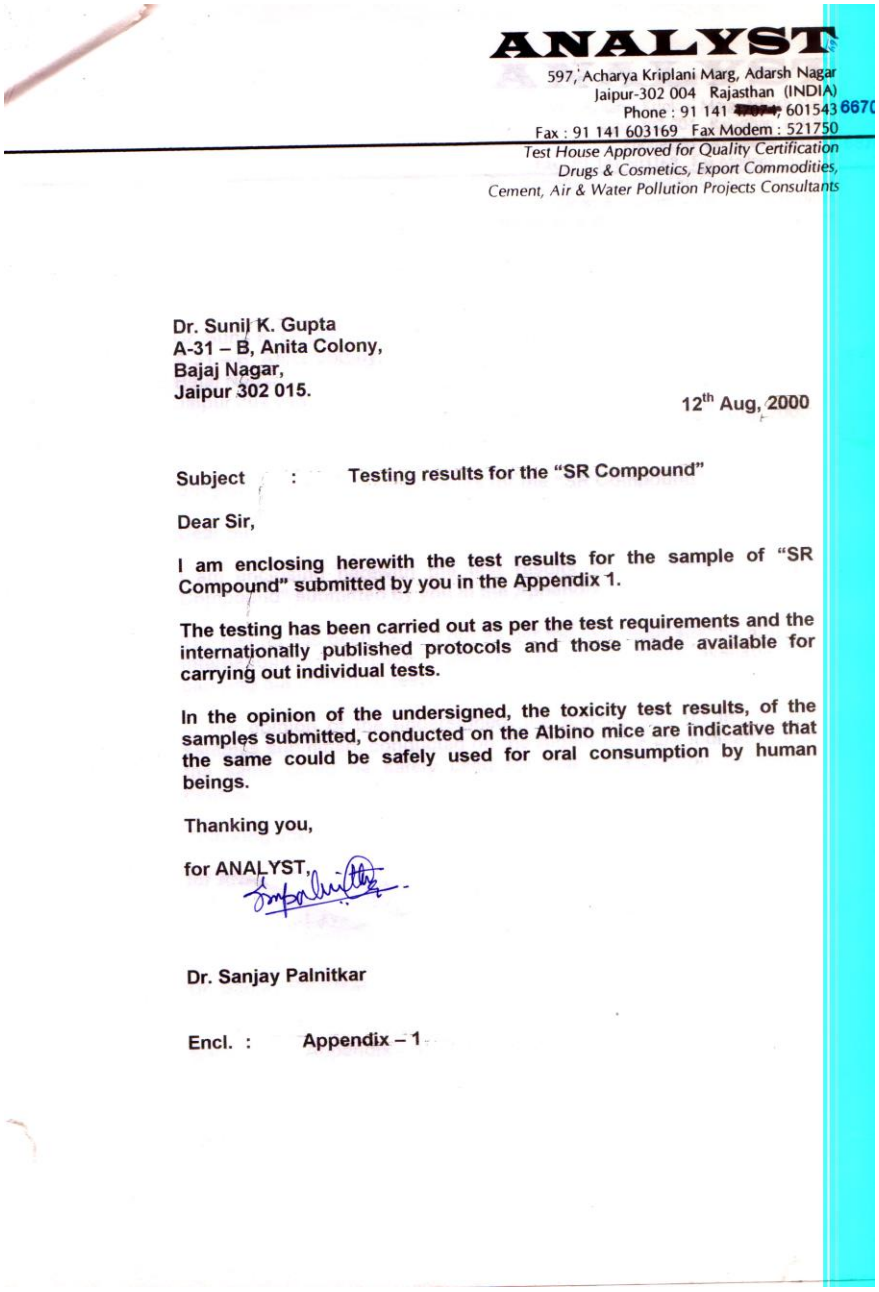



# 9 Safety Profile of the Treatment

- This formulation is safe for human consumption
- So far as about 700 cases of higher mental function disorders are consumed or consuming this supplement.
- This supplement does not contain any ingredients, which is in the exclusion list of the FDA.

The safety profile of herbal nutritional supplement is given as per following laboratory results**. Lately SR Compound has been renamed as CERBRO-FLO**



**ANALYST**

597, Acharya Kriplani Marg, Adarsh Nagar
Jaipur-302 004 Rajasthan (INDIA)
Phone : 91 141 [redacted] 601543 6670
Fax : 91 141 603169 Fax Modem : 521750
*Test House Approved for Quality Certification*
*Drugs & Cosmetics, Export Commodities,*
*Cement, Air & Water Pollution Projects Consultants*

Dr. Sunil K. Gupta
A-31 – B, Anita Colony,
Bajaj Nagar,
Jaipur 302 015.

12th Aug, 2000

Subject : Testing results for the "SR Compound"

Dear Sir,

I am enclosing herewith the test results for the sample of "SR Compound" submitted by you in the Appendix 1.

The testing has been carried out as per the test requirements and the internationally published protocols and those made available for carrying out individual tests.

In the opinion of the undersigned, the toxicity test results, of the samples submitted, conducted on the Albino mice are indicative that the same could be safely used for oral consumption by human beings.

Thanking you,

for ANALYST,

Dr. Sanjay Palnitkar

Encl. : Appendix – 1

## Humidity control Study for stability of "SR Compounds"

The following organisms will be tested for colony counts at 6 and 12 wk.:

| | | Initial | 6 Weeks | 12 Weeks |
|---|---|---|---|---|
| I. | E. coli/gm | Nil | Nil | Nil |
| II. | Salmonella /gm | Nil | Nil | Nil |
| III. | S. aureus /gm | Nil | Nil | Nil |
| IV. | Pseudomonas/gm | Nil | Nil | Nil |
| The others are | | | | |
| I. | yeast | Nil | 5/gm | 8/gm |
| II. | Molds | 8/gm | 13/gm | 25/gm |

## Animal Study for oral toxicity of "SR Compounds" on Albino mice

TEST REQUIREMENTS

Dose: Five times of the normal dose
25 times of the normal dose

Observation: Mortality of the animal

EXPERIMENTS PERFORMED

| | | |
|---|---|---|
| Normal Dose | : | 30 mg / Kg. of body weight |
| A] Dosage Administered | : | 150 mg./ Kg of body weight |
| Number of Sets | : | Dosage used on five sets of 6 Albion mice used |
| Method of Administration | : | Oral with milk ( 1: 10 v/v) |
| Mortality of Animal | : | |
| Immediately | : | Nil |
| After 4 Hrs | : | Nil |
| After 12 Hrs. | : | Nil |
| After 24 Hrs. | : | Nil |
| After 2 Days | : | Nil |
| After 5 days | : | Nil |
| After 10 days | : | Nil |

| | | |
|---|---|---|
| B] Dosage Administered | : | 7500 mg./ Kg of body weight |
| Number of Sets | : | Dosage used on five sets of 6 Albion mice used |
| Method of Administration | : | Oral with milk ( 1: 10 v/v) |
| Mortality of Animal | : | |
| Immediately | : | Nil |
| After 4 Hrs | : | Nil |
| After 12 Hrs. | : | Nil |
| After 24 Hrs. | : | Nil |
| After 2 Days | : | Nil |
| After 5 days | : | Nil |
| After 10 days | : | Nil |

**FOR ANALYST,**

12/08/2000

**C.J. MALHOTRA**
**(CHIEF CHEMIST)**

# APPENDIX – 1

## Studies for stability of "SR Compounds" & Accelerated temperature studies

The study will be conducted at Temperature variation of $45^0$ C

| Parameters | 0 Wk. | 3 Wk. | 6 Wk. | 9 Wk. | 12 Wk. |
|---|---|---|---|---|---|
| Volatile oils | 1.5%(W/W) | 1.47% | 1.42% | 1.40% | 1.31% |
| Water & Volatile matters | 7.90% | 7.5% | 7.10% | 7.01% | 6.82% |
| Extractable Matter | | | | | |
| Water | | | | | |
| Cold | 23.90% | 22.50% | 21.20% | 20.55% | 20.10% |
| Hot | 26.93% | 24.1% | 20.50% | 18.25% | 18.07% |
| Alcohol | | | | | |
| Cold | 15.0% | 14.4% | 13.50% | 13.0% | 15.8% |
| Hot | 16.0% | 15.54% | 14.58% | 13.89% | 12.8% |
| Ash | | | | | |
| - Total | 7.88% | 7.82% | 7.75% | 7.78% | 7.76% |
| - Acid insoluble | 1.39% | 1.30% | 1.34% | 1.32% | 1.38% |
| - Water soluble | 1.27% | 1.20% | 1.24% | 1.22% | 1.28% |

| | |
|---|---|
| Physical properties | |
| - Form | Powder |
| - Color | Greyish |
| - Odor | Characteristic |
| - pH | 5% w/v suspension – 6.27 |
| - Ignition Temp | 95 $^0$C |
| - Density | 1.0517 |
| - Solubility | Insoluble in water |

| | | |
|---|---|---|
| Heavy Metal | | Maximum Limit |
| - As | NIL | Max1.0ppm |
| - Pb | NIL | Max10ppm |
| - Cd | NIL | 3ppm |

# 10 Associated Documentation

## *Publications relating to cerebral perfusion*

### INTERNATIONAL REFEREED JOURNALS

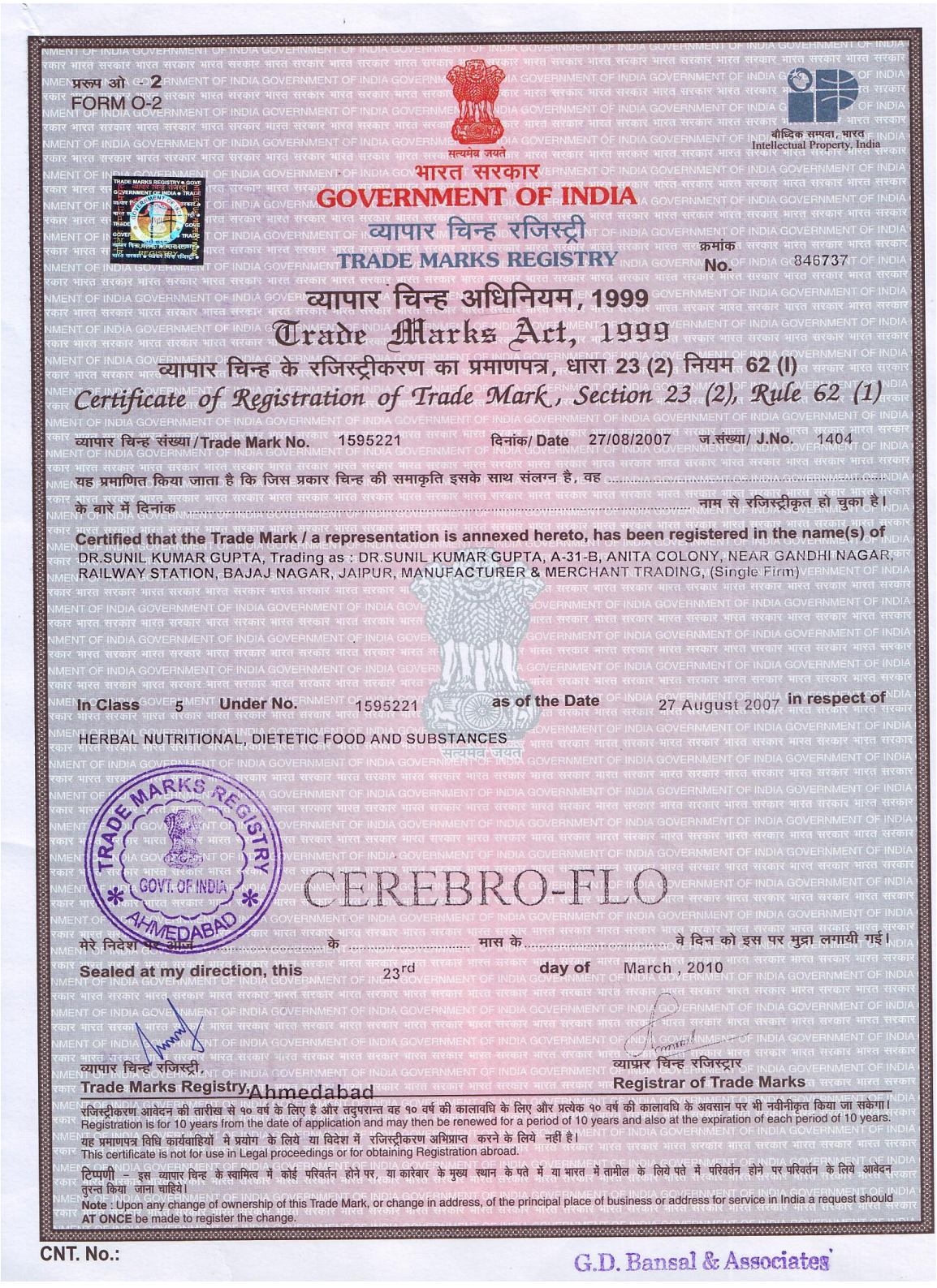
1. Gupta SK and Ratnam BV.Cerebral Perfusion Abnormalities in Cases of Down Syndrome: A SPECT Study. NRR, 2009 (not published yet)

### INDIAN JOURNAL

2. Gupta SK and Ratnam BV. Cerebral Perfusion Abnormalities in Children with Autism and Mental Retardation: A Segmental Quantitative SPECT Study. Indian Pediatrics, 2009; 46: 161-164.
3. Gupta SK. Improvement in cerebral perfusion abnormalities in cases of autism with herbal nutritional supplement - a segmental quantitative SPECT study. Ayuveda Prakash, Vol. 5 (4), April-june, 2008, 31-34.
4. *Improved Cerebral Perfusion Following Use Of "SR Compounds" In Mentally Retarded Children: A 99 Tc- Labeled HMPAO SPECT Studies Of Brain. Paper presented at V International Congress of tropical pediatrics, Feb. 10-15, 1999, Jaipur. Abstract of the paper was published in the proceedings.*
5. *Gupta SK and Ratnam BV. Cerebral Perfusion Abnormalities in Cases of Down Syndrome. Indian Pediatrics, 2011; 48: 70-71s.*

# 11 Trademark Certification

**CEREBRO-FLO i.e. SR COMPOUND**



प्ररूप ओ - 2
FORM O-2

बौध्दिक सम्पदा, भारत
Intellectual Property, India

सत्यमेव जयते
भारत सरकार
GOVERNMENT OF INDIA
व्यापार चिन्ह रजिस्ट्री
TRADE MARKS REGISTRY

क्रमांक No. 846737

व्यापार चिन्ह अधिनियम, 1999
Trade Marks Act, 1999

व्यापार चिन्ह के रजिस्ट्रीकरण का प्रमाणपत्र, धारा 23 (2) नियम 62 (I)
*Certificate of Registration of Trade Mark, Section 23 (2), Rule 62 (1)*

व्यापार चिन्ह संख्या / Trade Mark No. 1595221 दिनांक/ Date 27/08/2007 ज.संख्या/ J.No. 1404

यह प्रमाणित किया जाता है कि जिस प्रकार चिन्ह की समाकृति इसके साथ संलग्न है, वह ..... नाम से रजिस्ट्रीकृत हो चुका है।
के बारे में दिनांक .....

**Certified that the Trade Mark / a representation is annexed hereto, has been registered in the name(s) of**
DR.SUNIL KUMAR GUPTA, Trading as : DR.SUNIL KUMAR GUPTA, A-31-B, ANITA COLONY, NEAR GANDHI NAGAR, RAILWAY STATION, BAJAJ NAGAR, JAIPUR, MANUFACTURER & MERCHANT TRADING, (Single Firm)

**In Class** 5 **Under No.** 1595221 **as of the Date** 27 August 2007 **in respect of**

HERBAL NUTRITIONAL, DIETETIC FOOD AND SUBSTANCES

TRADE MARKS REGISTRY * GOVT. OF INDIA * AHMEDABAD

CEREBRO-FLO

मेरे निदेश पर आज ..... के ..... मास के ..... वे दिन को इस पर मुद्रा लगायी गई।

**Sealed at my direction, this** 23rd **day of** March , 2010

व्यापार चिन्ह रजिस्ट्री,
**Trade Marks Registry, Ahmedabad**

व्याप्रार चिन्ह रजिस्ट्रार
**Registrar of Trade Marks**

रजिस्ट्रीकरण आवेदन की तारीख से १० वर्ष के लिए है और तदुपरान्त वह १० वर्ष की कालावधि के लिए और प्रत्येक १० वर्ष की कालावधि के अवसान पर भी नवीनीकृत किया जा सकेगा।
Registration is for 10 years from the date of application and may then be renewed for a period of 10 years and also at the expiration of each period of 10 years.

यह प्रमाणपत्र विधि कार्यवाहियों मे प्रयोग के लिये या विदेश में रजिस्ट्रीकरण अभिप्राप्त करने के लिये नहीं है।
This certificate is not for use in Legal proceedings or for obtaining Registration abroad.

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**Note** : Upon any change of ownership of this Trade Mark, or change in address, of the principal place of business or address for service in India a request should **AT ONCE** be made to register the change.

**CNT. No.:**

G.D. Bansal & Associates

# 12 Resume of Dr. Sunil Kr Gupta


| | | |
|---|---|---|
| **Name** | : | Dr. SUNIL Kr. GUPTA |
| **Designation** | : | 1.Consultant Pediatrician & Neonatologist<br>2. Chief Scientist of Environmental Medicine (Including Environmental Health) |
| **Institution** | : | AAY Research Centre C/O Krishna Ram Hospital and Research Centre |
| | : | A-31B, Anita Colony, Bajaj Nagar, JAIPUR-15<br>Tel : 91-141-271-0055<br>Mobile : 91- 941-404-2000<br>Email : drsunil@gmail.com |
| **Educational qualifications** | : | MBBS, MD (Paed.Med.), Ph.D. |
| **Professional Societies Membership** | : | Life Member, Indian Academy of Pediatrics; Indian Medical Association |


**Research specialization (major scientific field(s)of interest):**

a. **Mental Retardation, Down's syndrome, Autism**
b. **Immune disorders:** Juvenile Rheumatoid arthritis, Nephrotic syndrome, Immune thrombocytopenic purpura
b. **Fluorosis**: Research out treatment of fluorosis, Development of new defluoridation process (KRASS process) and Development of new tooth powder, useful to remove the dental stains
c. **Nitrates**: Extensive research work on human health hazards of Nitrate in drinking water. Many International publications are there.

**Work & Teaching Experience:** Consultant Pediatrician & Neonatologist, Research Guide for ME students, Teaching to graduate and post graduate students: Reviewer of international journals, Taking lectures regularly

**Awards:** Many National and international academic awards

**Research Projects:** Successfully carried out 9 research project as PI. The projects were sponsored by DST, CSIR, SMS Medical College and NEERI

**Publications**

**Books:** Chapter in 4 books (One chapter in each book)
Book on nitrate and human health
Monograph on fluoride
**International:** 14 papers have been published in International journals
**National:** 34 papers published in National Journals
**International and National conferences:** 17 papers published and presented