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EFFICACY OF HOMOEOPATHIC MEDICINE CALADIUM SEGUINUM IN TOBACCO DE ADDICTION AND REHABILITATION

1 . INTRODUCTION

Tobacco , a plant native to the North Americas which was primitively introduced into the world as a medication slowly and deeply grew its roots to become on of the strongest addiction of man around the world. Tobacco dependence can be defined as ," Cluster of behavioral, cognitive and physiological phenomena that develop after repeated tobacco use and that typically include a strong desire to use tobacco , difficulties in controlling its use , persistence in tobacco use despite harmful consequences"[1].

Tobacco is responsible for about 5 million deaths per year. More than one out of three adults in India use tobacco in any form showing a male prevalence of about 42.4% over 14.2% consumption by females population and is a prim reason for about 1 million death per year in India.The addiction and overuse of the substance has serious effects on almost all organs of the human body leading to declining health, quality of life and death[2][3][4].

Tobacco addiction can be categorized as the over and uncontrollable usage of tobacco despite the knowledge of adverse effects of health. Tobacco cessation is a difficult process due to the existence of an array of withdrawal symptoms ranging from craving for nicotine to mental conditions depression and anxiety.

Most of the modern tobacco rehabilitation techniques include Nicotine Replacement Therapy, where nicotine induced medication and chewing gums which provides the patient with an alternative source of nicotine, thus causing aversion to tobacco. Unfortunately, nicotine is what keeps smokers smoking. Simply nicotine poisoning happens when we have too much of it in your body relative to your body weight. Overdosing from nicotine gum or a patch is rare, but it's possible if you don't follow the instructions carefully.

Previous homeopathic studies have brought light of the efficacy of Homoepathic medication in substance abuses in both alcoholism and tobacco and their control of withdrawal symptoms.The major component of this study is the implementation of Homoeopathic treatment for tobacco addiction. While conventional pharmacological and behavioral treatments are effective in improving cessation success, the rate of relapse to tobacco use remains high, demonstrating the strong addictive nature of nicotine.

Homoeopathic preparation of Caladium seguinum is having profound action on removing craving for tobacco. The drug is indicated as it **"Destroys the cravings for tobacco"**[5].The unique benefit that the homoeopathic medicine provide is by strengthening the person's constitution so that they become less addicted to tobacco but also make them emotionally stronger and thus feel less socially addicted to what tobacco represents to them.

SIGNIFICANCE OF THE STUDY

On successfully getting this study done a new and homoeopathic way of getting rid of the everlasting tobacco addiction may be made possible. This also paves way to a type of de-addictive measure without supplementation of nicotine ,which is indirectly a cardiac poison once it meets its level of toxicity. This also may give the patients a more economic or cost effective way for tobacco de addiction , an easy management of withdrawal symptoms and a long standing or permanent escape from this ravaging addciction. The study also help to leave a mark in extending the ever increasing knowledge of homoeopathy in general and specifically in the field of substance abuse and management of addictions.

AIM OF THE STUDY :

The ultimate aim of the research is to check the effectiveness of caladium seguinum 30 C and 200 C in tobacco de-addcition and rehabilitation with facile management of withdrawal symptoms.

OBJECTIVES OF THE STUDY:

Primary objective

1. To study about the action of Caladium seguinum in tobacco users with the potencies 30C and 200C.

2. To do a comparative study within the action of various potencies of Caladium seguinum.

3. To find a better and effective way for managing the withdrawal symptoms of tobacco

Secondary objective

1. To initiate a non-nicotine dependent treatment plan to rehabilitate the tobacco addicts.

3. To expand the existing knowledge of Homoeopathy in

REVIEW OF LITERATURE

TOBACCO PLANT

Tobacco is a pereneal and pubescent herb belonging to the family of solnaceae originally native to America but is vastly cultivated throughout the globe with common names being Fumo , petume , petina , etum and tabaco etc. It may about a height of 9.0 - 1.50 meters with large anceolate green leaves, trumpet shaped pinkish flowers and all parts of the plant has a wide supply of gladular hair like appendages secreting the major alkaloid , Nicotine , hence renderiig all parts of the plants poisonous except for the seeds[6][7].

TAXONOMY

Scientific name:	**Nicotiana Tabacum Linn.**
Kingdom	**Plantae, Eudicots, Asterids**
Division	**Magnoliophyta**
Class:	**Magnoliopsida**
Order	**Solanales**
Family	**Solanaceae**
Genus	**Nicotiana**
Species	**Nicotiana tabacum**

ALKALOIDS IN TOBACCO

Major : Nicotine
Minor : Nicotoine , nicotenine , icotellube ,
Isonicoteine ,Nicotimine ,Anabasine ,
l-Anabasine , Nicotyrine .l-Notnicotine[9].

NICOTINE

Nicotine was primitively considered as the only alkaloid present in tobacco until the above mentioned minor or lesser were isolated. Nicotine is present in all parts of the plan with the greater amounts concentrated in lower leaves. The nicotine content of the plant increased with the aging of the plant.Commercial extraction of nicotine is done by stream distillation after alkali treatment.Nicotine is odourless white liquid which produces a burning taste in the mouth and is inflammable in air in its vapour form[9].

TOXICOLOGICAL EFFECTS OF NICOTINE

Toxic levels of Nicotine targets ganglionic sites and motor end plates.Cardiovascular and Central Nervous systems are the major site of action leading to spasms and convulsion , with mental depression and progressing to respiratory arrest and death.

Pure nicotine poisoning leads to rapid decline in health leading to death within Minutes of ingestion. Delayed poisoning as from injestion of leaves can lead to sever abdominal pain , diarrhoea and cold sweat , mental confusion and trouble in coordination . hypertension and tachypnoea followed by depression in both then to collapse and death[10].

TOBACCO AND INDIA

In India almost all states cultivated over 60 sub species of Nicotiana and with Andhrapradesh ,Gujarath and TamilNadu leading the market. Below mentioned and some varieties of strains cultivated in India with respective industrial uses :

Bidi: Keliu-49, Keliu-20, Surati-20, Anand-2, Anand-3, Kunkumathiri

Cigar filler: OL-10, VV-2, KV-1, I-462

Chewing: I-64, PV-7, WR-2, I-115, VTK-1, VD-1

Hookah: N.P.70, N.P.35, D.P.401, D.D.413[8].

India is 2nd among the global leader of tobacco production and is the 3rd larger exporter with a massive export value of 60.84Bn as per reports of 2018 financial year. Tobacco is mainly harvested in two forms , cigarette and non - cigarette with the non cigarette products having market share of 69% of the whole tobacco market [11].

India ranks 2nd in consumption of tobacco with 276 million and 200 million indulging in smoking and smokeless use of tobacco estimating a global share of 12% in tobacco usage. Indian numbers for deaths using smokeless tobacco usage is equals to about 3/4th of that of the whole world[11].

People using tobacco in India averages from the age of 22 to 45 with adolescence marking the common period of initiation with a male predominance ratio of around 19 : 2 too that of women[12][13][14].

FORMS OF TOBACCO INTAKE

There are various forms in which nicotine enter s our body and the effects of nicotine varies in their intesity depending on the mode of intake. The forms of intake can be classified into two groups , combustible and non combustible[15][16].

COMBUSTIBLE FORM

- Cigarettes
- Bidi
- Cigars And Pipes
- Hookah

NON COMBUSTIBLE FORMS

- Tobacco Chewing
- Snuff
- Dissolvables

E CIGARETTES

NICOTINE CONTENT

A Cigarette on average contain about 10mg of nicotine. Cigars can have nicotine content ranging from 10 to 300 mg. Bidis are said to have around 21mg to per gram of tobacco.A water piper of Hookah is said to have around 20g of nicotine. On an average moist stuff amounts to contain 16mg of nicotine per gram of tobacco[17].

HYSTORY OF TOBACCO SMOKING

Smoking at first was a symbol of glamour ,maturity and manliness which promised immanence pleasure after the initial stages of repulsion. It was spread to the masses by commercial advertising and television.With more and more inventions like E cigarettes emerge claiming themselves healthier than conventional cigarette smoking has lead to the increasing demand or addiction to the habit of smoking at younger ages throughout the world[17][18].

TOBACCO ADDCITION AND WITHDRAWAL

The main ingredient that leads to addiction to tobacco is Nicotine , “it is what keeps smokers smoking”which is more addictive than cocaine and many other drugs. Main reason for this ever increasing addiction is due to the stimulating and sometimes depressive action of nicotine. Nicotine stimulates alertness, attention , memory processing and even learning and also boosts mood and promotes pleasure and reduces anger and mental tension.

The compound of nicotine mimics the structure of Acetylcholine and thus get detected at cholinergic receptors of our body thus end up activating dopamine ,nor epinephrine , vasopressin and serotonin which leads to the above mentioned behavioral alterations. Thus the brain brings up further requirement of nicotine to promote he conditions and thus leads to addiction[15][19].

CRITERIA FOR ADDICTION

A person may be classified as an addict of nicotine if he satisfies any two instances from the following criteria in a period of 12 months .

1. Consumption in any form over a longer period or often taking large amounts.
2. Recurrent desire and attempts to quitting , often ending in vain.
3. Immense time spent or activities done to attain tobacco
4. Tobacco use restricting to carry out major activities of work school or home completely and punctually.
5. Craving or urge to use tobacco.
6. Continued use of even after serious arguments , social and personal problems cause due to habit of tobacco usage.

7. Giving up or reduced involvement important social , occupational and recreational activities because of tobacco use.
8. Usage in physically hazardous situations.
9. Persistent usage after knowing the deleterious effects of continued usage.
10. Tolerance (Requirement of increasing amounts to attain the desired effect / diminished effect due to use of same amount of tobacco) [18][19].

WITHDRAWAL SYMPROMS

As the physiology of the addict's body adapts with nicotine it requires recurrent supply of nicotine and when consumption is arrested abruptly it brings out withdrawal symptoms which makes it hard to quit tobacco.They may appear and intensify within the first 24 to 48 hours of cessation of tobacco.These symptoms may include :-

- Increased Craving
- Restlessness
- Anxiety and impatience
- Irritability
- Lack of concentration and disorientation
- Dizziness and headaches
- Gastric problems and overeating
- Insomnia
- Palpitation and tremors

And these may persists even after months of cessation even if successfully possible to attain cessation. This makes quitting so hard and breaks people even with immense desire and forces them to go back to tobacco usage[15][19].

HARMFULL EFFECTS OF TOBACCO ON HEALTH

Tobacco usage kills around 5 million people per year globally and around 1 million deaths per year in India.The major factors leading to deaths can be Cardiovascular , pulmonary or carcinogenic effects [20].

CARDIOVASCULAR

Cardiovascular diseases lead to most deaths than the other two ranging to around 40% of the total death in the country .Smoking induces production of Low Density Lipoproties thus leading to atherosclerosis and vascular damage .Tobacco increases heart rate by sympathetic excitation or paralysis of parasympathetic cardiac ganglia, Hypertension , reduction in coronary vascular resistance , tobacco induced angina pectoris[15][20].

RESPIRATORY EFFECTS AND CANCER

Chronic obstructive lung diseases has listed tobacco has one of the most common and major etiologies mainly Emphysema.It leads to many pulmonary infections mainly tuberculosis which has fatal end results.More than 50%of the cancers are originated due to tobacco usage.The major site of cancer are oral cavity , lungs, pharynx and oesophagus[15][20].

PREGNANCY RELATED EFFECTS

Long term tobacco usage and usage in pregnant women can lead to Bleeding ,Ectopic pregnancy,Miscarriage,Premature birth /Still Birth and Placental Abnormalities[20[20][21]].

OTHER EFFECTS

Low emotional stability
Neonatal disorders
Rheumatic conditions
Diabetes
Dental caries
Inflammatory Bowel Diseases
Erectile dysfunction[22][23][24]

NICOTINE REPLACEMENT THERAPY (NRT)

Nicotine Replacement Therapy is method of temporary replacement of nicotine source like tobacco products tending to reduce the harmful effects , especially withdrawal symptoms and thus leading to an easy de-addcition from tobacco.It

focuses on rapid delivery of nicotine and even by vaccination methods to tackle dependence[22]. These alternative nicotine sources can be :

- **Gums** : Intermittently chewed and held in mouth for about 30 minutes ranging from a dosage of 2 to 4 mg of nicotine.
- **Trans-dermal Patches** : especially targeted for highly depended subjects which can subdermally supply large doses of nicotine ranging between 5m to 22mg.
- **Nasal Sprays**: Targeted for rapid delivery of nicotine with dosages upto 40 per day delivering 0.5mg per 50ul spray squirt.
- **Inhalers :** Oral inhalers that supplement which also target to reduce the "hand to mouth ritual " of smoking and nicotine content can range from 2mg to 10 mg.
- **Sub lingual Tablets** : Non chewable tablets of nicotine ranging up to 2mg
- **Electronic Nicotine Delivery System / E-cigarettes :** Promotes vaporization of chemical mixture containing nicotine and delivers it directly to pulmonary mucosa with content varying between 1 -34mg/ml.
- **Nicotine Vaccines :** Most modern method under testing which can render the immune system to detect nicotine as a foreign object producing antibodies to tackle it[25].

SIDE FFECTS OF NICOTINE REPACEMENT THERAPIES

Researches have identified that side effects can exits, even though they couldn't be completely proved on extend and severity due to lack of evidence but the probability of such effects must not be seen lightly.The serious health effects of nicotine replacement therapy can be :

- Respiratory Abnormalities
- Cardiovascular diseases
- Stroke
- Pregnancy Related Complaints
- Neonatal Complaints[26][27]

CALADIUM SEGUINUM

Synonyms : Caladium vent , Aurum Seguinum Linn ,

Natural order : Araceae

Common names : Dumb cane , Poison American Aurum ,
Posionous Pediveau

Habitat : South America , Wet prairies of Paramaribo.

Steam : 5-6ft tall , 1 inch thick
Round,knotty containing Milky juice

Leaves : Oval - oblong , smooth with narrow apex

Proved by : Dr.Constantine Herring

Part used : Fresh root

Dilutions to be prepared
Under: Class III[29]

INDICATIONS OF CALADIUM

The indications mentioned below are considered as the basis of remedy selection for the study as it covers most of these symptoms occurring due to prolonged tobacco usage and also the withdrawal symptoms

General : Destroys the craving for tobacco.An exceedingly healthy feeling appeared after twelve or twenty-four hours

Mind : Low spirit , Irritability , Depression , Lack of Concentration .

Head : Headache with nausea. Headache and mental states of smokers.

Eyes : Sensitive, stupefying pressure in the eyes and forehead, with heat in the face,and restlessness he can hardly control, while smoking tobacco;

Ears : very sensitive to noise

Stomach : Acrid eructations,sensation as if full by dry food,Sensation of hunger, soon after taking,Takes his breakfast with hunger and relish, but is hardly satisfied when he becomes discouraged and uncomfortable.

Stool : Hard lumpy stools and burning ,Seven stools, at first watery, afterward thicker

Male sexual organs : Impotence with mental depression, penis remains relaxed.

Respiratory : Impedes deep breathing , oppression of breathing , Catarrhal asthma,great oppression of the chest, so that he could scarcely get the breath

Heart : Tobacco heart ,Stitches up chest,A peculiar throbbing below the heart

Extremities : Rheumatic Pains

Sleep : Sleepless or Unrefreshing sleep[5][30][31][32].

METHODOLOGY

INCLUSION CRITERIA

- Age group 20 to 45 years
- Persons using tobacco in any form
- Persons volunteering to give up tobacco use

EXCLUSION CRITERIA

- Persons diagnosed with chronic respiratory, cardiac conditions and malignancy.
- Age group below 20 years and above 45 years
- Person under quarantine or tested positive for COVID19 viral infection.
- Subjects diagnosed with any ulcerate buccal pathology

SAMPLE SELECTION

Method: Purposive sampling

STUDY DESIGN

Online Screening Programme with Web based form

A Google Survey Form was created and was published in the social media for screening of around 200 individuals for the Tobacco De addcition programme.

Contents of the form

- Questionnaire model of Fagerstrom Test for Nicotine Dependence
- Questions enquiring the dependence on tobacco during Covid19 Pandemic
- Invitation to join the Homeopathic Tobacco De-addiction Programme
- Enquiry for Name , Address and Contact information of those willing to attend the programme

Tobacco Awareness and Administration of Medicine

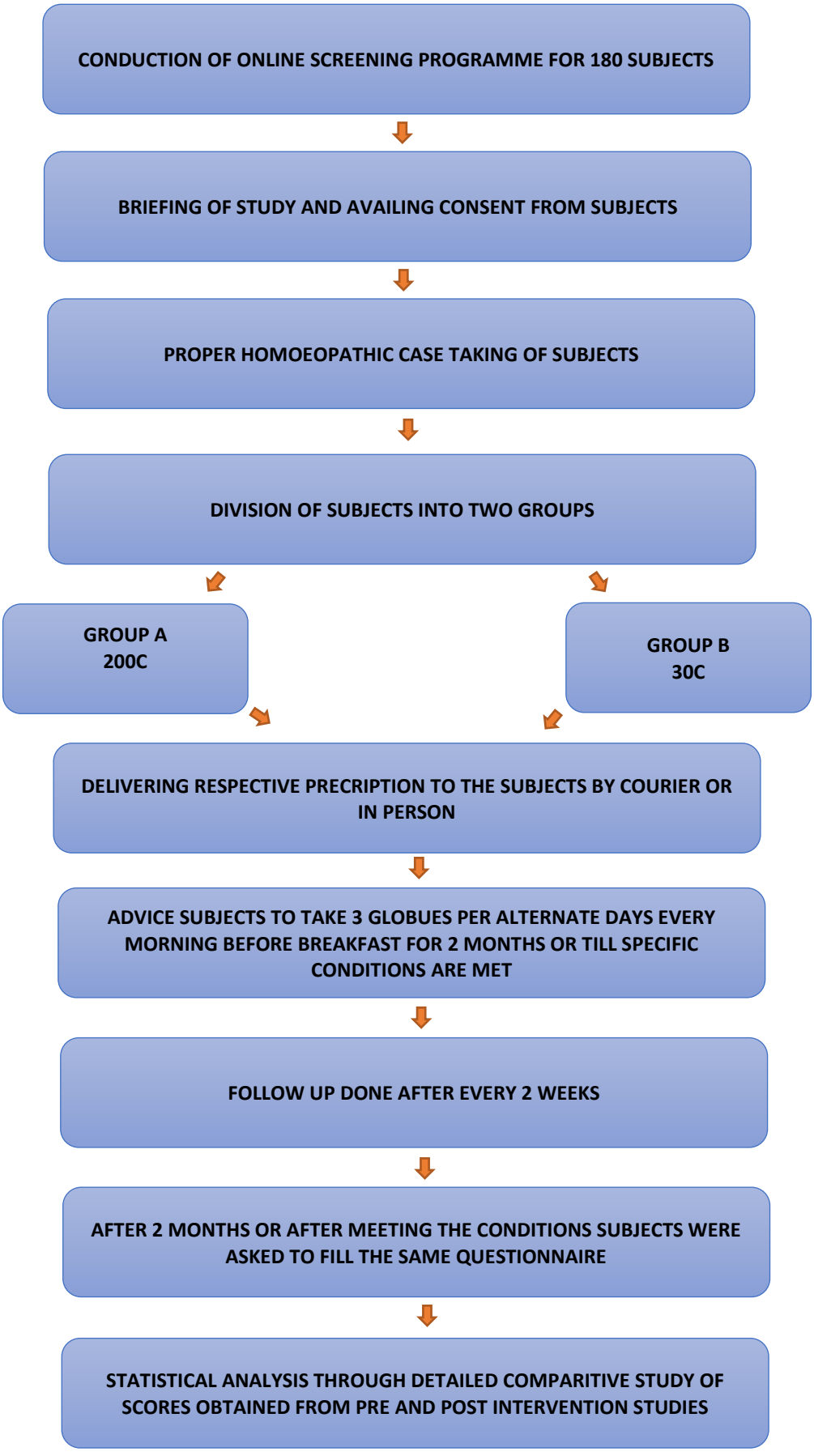
- Collection of online and responses were done and graphical representation of the available data was made.
- Sampling was done and subjects were briefed about the programme and was made aware of the after effects of long term tobacco usage , the methodology of the study and about the withdrawal symptoms.
- Consent form was mailed to the people willing to join the programme with proper contact information.

- Proper Homeopathic case taking was done and recorded for those you willed to attend the programme.
- Medicine was prescribed and delivered by courier or in person to the subjects.
- Subjects were divided into 2 halves/batches and Caladium seguinum 200C and 30C were given to the Batch1 and Batch 2.
- Method of administration was advised as 3 medicated globules per alternate days before food in the morning.
- Subjects were asked to follow the administration schema for a period of 2 months and to report any symptom that develops and were asked to pursue their routine lifestyle
- Patient status and follow up was done every 2 weeks and findings were logged.
- At the end of 2 months , subjects were asked to fill the same questionnaire and results were obtained.
- Results from the Pre and Post questionnaires were compared.
- Observation was done ,Graphical representation and statistical analysis of final result was made.

FAGERSTORM TEST FOR NICOTINE DEPENDENCE (FTND) : DEPENDENCE LEVEL TABLE

FTND SCORE	DEPENDENCE LEVEL
0-2	Very Low
3-4	Low
5	Medium
6-7	High
8-9	Very High

METHODOLOGY FLOWCHART



MANAGEMENT STRATEGY FOR WITHDRAWAL SYMPTOMS

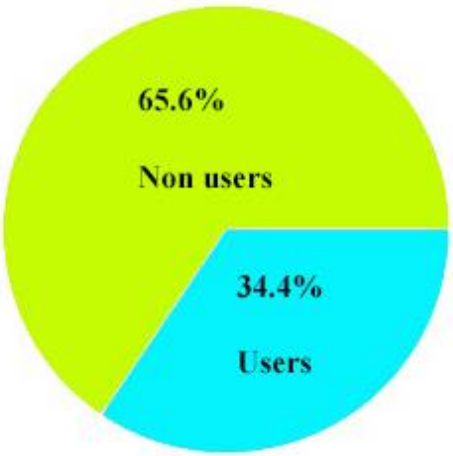
Increased craving for smoking (hand to mouth ritual)	**: Advised to blow through paper Straw or Empty Pen mimicking smoking**
Fatigue	**: Increase fluid intake , Take rest**
Sleeplessness	**: Avoid Tea , coffee , Advised to read books.**
Cough	**: Fluid intake**
Dizziness	**: Slow changes in position , Advised to take more fruit / vegetables**
Lack of concentration	**: Advised to small activities, to plan work load ,keep a time table , adviced to do mentally rewarding tasks.**
Constipation	**: Fibrous diet and Fluid intake**
Headache	**:Rest and fluid intake**
Depression or gloominess	**:Directly Share with the researcher or loved ones.**

OBSERVATIONS AND RESULTS

SUVERVEY OUTCOME

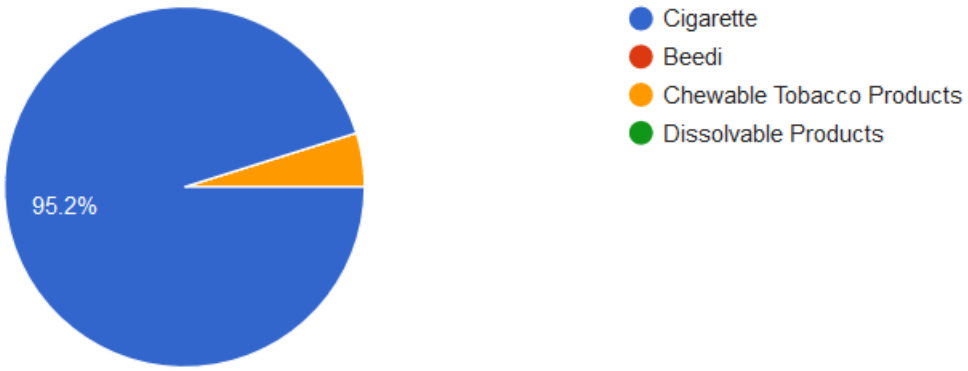
- **Tobacco usage in screened subjects (Total 180 subjects)**

Users : 62/180
Non Users : 118/ 180



- **Tobacco usage in forms :**

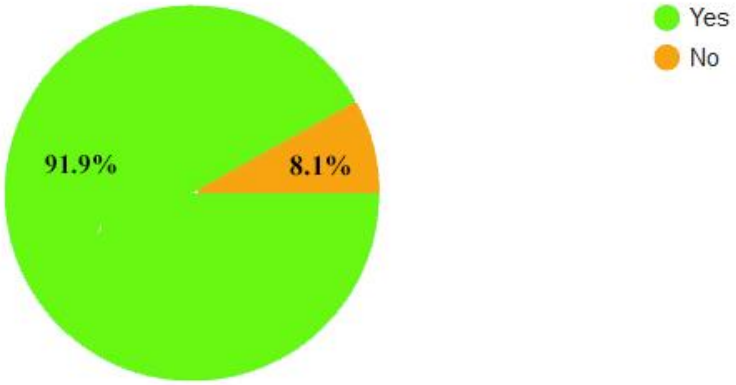
Cigarettes : 95.2%
Chewable Forms : 4.8 %



- **Awareness about harmful effects of tobacco (Total 62 Users)**

  91.9 % of the Users were well aware.

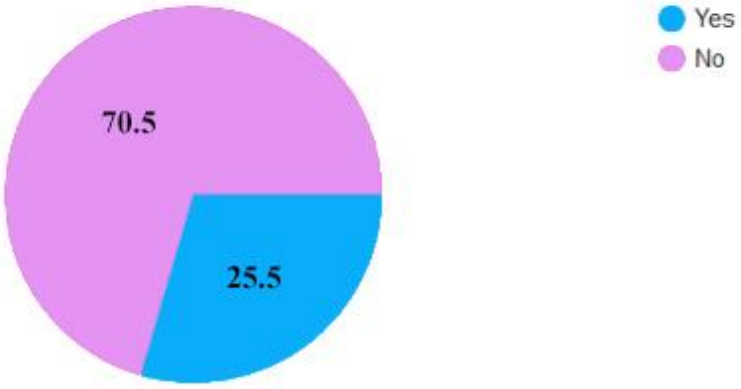
  Only 60.7% wish to stop smoking.



- **Increased Dependence on Tobacco during the COVID 19 lockdown periods(Total 62).**

  29.5% has increased dependence.

  70.5% has decreased dependence.



SAMPLING OUTCOME

Number of positive responses for the test : 15

Numbers selected after selection criteria : 12

CLASSIFICATION OF SUBJECTS

BASED OF FAGERSTORM TEST

POINTS	DEPENDENCE LEVEL	NO OF SUBJECTS
7-10	HIGH	3
4-6	MODERATE	5
<4	MILD	4

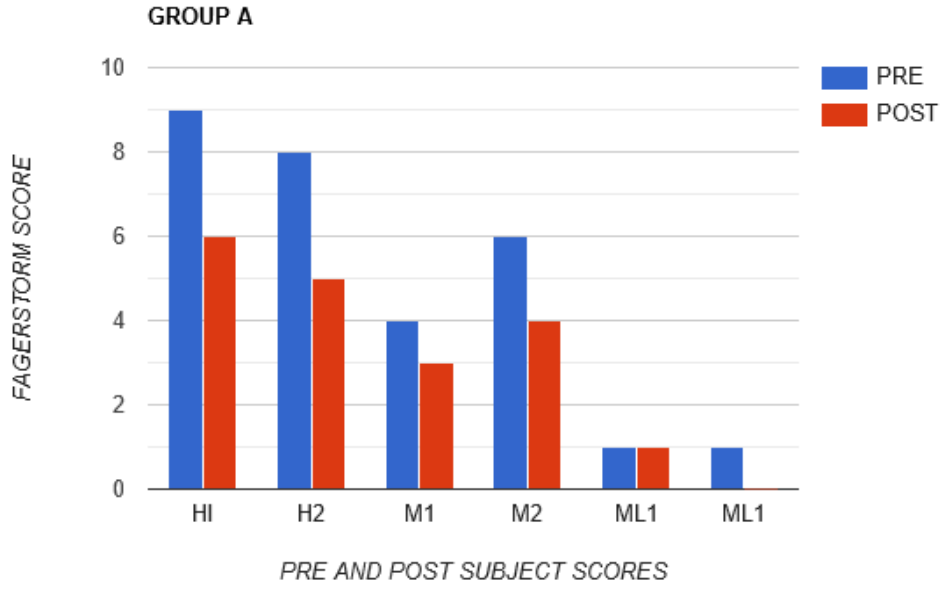
GROUPING OF SUBJECTS

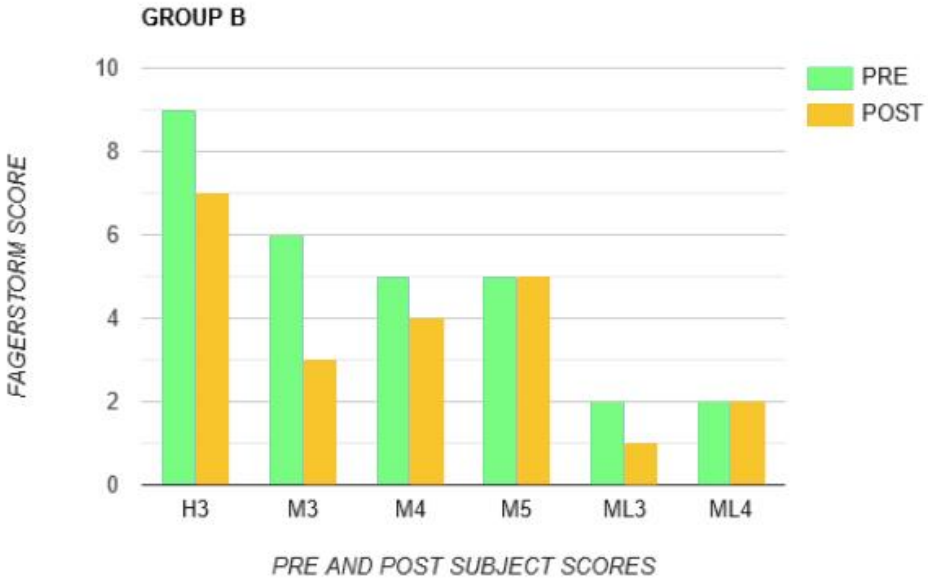
GROUP	NUMBER OF SUBJECTS	POTENCY
Group A	2 High + 2 Moderate+ 2 Mild	200 C
Group B	1 High 3 Moderate And 2 Mild	30 C

TREATMENT OUTCOME

- Subjects with high and moderate tobacco dependence showed decreased level of dependence post study based in Fagerstorm score.
- Mildly dependant subjects were found to be less adhesive to the treatment.
- Highly dependant subjects experienced sudden decline in craving than the moderate and mild dependant subjects.
- Withdrawal symptoms were easily and effectively managed in the Higher and Moderately dependant subjects than mildly dependant.
- Both 200C and 30C potencies were successfully found effective in reducing the craving for tobacco for those who strictly adhered to the treatment.

GRAPHICAL COMPARISON OF PRE AND POST FAGERSTORM SCORE





(H=High , M=medium , ML=mild subjects followed by numbering according to chronology of application for the study)

Group A - 200c	**Before**	**After**
Mean	4.83	3.33

Group B -30 C	**Before**	**After**
Mean	4.83	3.66

STATISTICAL ANALYSIS

For Group A prescribed with 200C potency the mean average before the treatment was 4.83 and after the treatment the mean average tobacco dependency of the sample fell to 3.33 and For Group B A prescribed with 30C potency the mean average before the treatment was 4.83 and after the treatment the mean average tobacco dependency of the sample fell to 3.66.

The fall in tobacco dependency is can be attributed to the efficacy of *Cladium seguinum* 200C and 30C potencies.

DISCUSSION

In this study it was found that out of 12 subjects 8 showed decline in tobacco dependence score while 2 subjects (M5 and ML2) showed no change and 2 subjects belonging to mildly dependant group found it difficult to adhere to the treatment plan. All subjects except one who were prescribed 200C potency and except one prescribed with 30C potency and strictly adhere to the treatment found reduction in their dependency and found it effective in managing the withdrawal symptoms.Only subjects using Cigarettes and Chewable tobacco enrolled in the study and was found effective under Homoeopathic medication.

Limitations

This study could have been employed in a more wide and effective way if the following limitations were met.

- Inability to perform a Tobacco Awareness and Deaddcition medical camp due to the ongoing COVID19 pandemic and its community restrictions as credibility of an online survey form was found to be doubtful and hence was unable to obtain a larger sample size.
- Proper patient management and guidance under direct supervision was unable due to the above mentioned reason,which gave way to improper adhesion to the treatment plan.
- A wider study based on different forms of tobacco could not be conducted.

CONCLUSION

The results of the study confirms that Homeopathic medication *Caladium seguinum* is effective in reducing the Craving for tobacco and also for the better management of the withdrawal symptoms of tobacco cessation and reinstate that the proving of Homoeopathic Pioneers were found to be true and useful. This also paves way for a new type of de-addiction of tobacco where the patients need not rely on continuous intake of nicotine which is indirectly harmful to the body. Detailed studies may be done to widen the scope of homoeopathy in the stream of de-addiction and substance abuse and save people from this devastating addiction.

REFERENCES

1. Seccion Toxicologia Hospital de Clinicas "José de San Martin" Cordoba 2351 1120 Capital Federal Argentina, D., 1998. Nicotiana Tabacum L (PIM 371). [online] Inchem.org. Available at: <http://www.inchem.org/documents/pims/plant/nicotab.htm#SectionTitle:1.2%20Family> [Accessed 14 September 2020].

2. Gajalakshmi V, Peto R, Kanaka T, Jha P. Smoking and mortality from tuberculosis and other diseases in India: retrospective study of 43 000 adult male deaths and 35 000 controls. The Lancet. 2003;362(9383):507-515.

3.Prof. Jugal Kishore, Department of Community Medicine, Maulana Azad Medical College on 27/10/2014 Effects of Tobacco on Health | National Health Portal of India [Internet]. Nhp.gov.in. 2010 [cited 2019 Aug 3]. Available from: https://www.nhp.gov.in/effects-of-tobacco-on-health_pg

4. WHO report on the global tobacco epidemic 2008 [Internet]. World Health Organization. 2020 [cited 23 September 2020]. Available from: https://www.who.int/tobacco/mpower/2008/en/

5. CALADIUM SEGUINUM - HOMOEOPATHIC MATERIA MEDICA - By William BOERICKE [Internet]. Homeoint.org. 2020 [cited 23 September 2020]. Available from: http://www.homeoint.org/books/boericmm/c/calad.htm

6. Kishore K. MONOGRAPH OF TOBACCO (NICOTIANA TABACUM) [Internet]. Semanticscholar.org. 2020 [cited 14 September 2020]. Available from: https://www.semanticscholar.org/paper/MONOGRAPH-OF-TOBACCO-(-NICOTIANA-TABACUM-)-Kishore/b1e005b9fd6985ba166298e0a5dbd40ebaec13b0

7 .Nicotiana tabacum L (PIM 371) [Internet]. Inchem.org. 2020 [cited 23 September 2020].Availablefrom:http://www.inchem.org/documents/pims/plant/nicotab.htm#SectionTitle:1.2%20Family

8. Agriculture Information | Crop information | Tobacco [Internet]. Indiaagronet.com. 2020 [cited 23 September 2020]. Available from: https://www.indiaagronet.com/indiaagronet/crop%20info/tobacco.htm

9 .Alkaloids of Tobacco. [Internet]. Pubs.acs.org. 2020 [cited 23 September 2020]. Available from: https://pubs.acs.org/doi/abs/10.1021/cr60092a004

10. Benowitz N. L. (1996). Pharmacology of nicotine: addiction and therapeutics. Annual review of pharmacology and toxicology, 36, 597–613. https://doi.org/10.1146/annurev.pa.36.040196.003121

11. ltd R. Tobacco Market in India (2018-2023) - Research and Markets [Internet]. Researchandmarkets.com. 2020 [cited 23 September 2020]. Available from: https://www.researchandmarkets.com/research/3mkchc/the_tobacco?w=4%20%20ID:%204757741

12. ltd R. Tobacco Market in India (2018-2023) - Research and Markets [Internet]. Researchandmarkets.com. 2020 [cited 23 September 2020]. Available from: https://www.researchandmarkets.com/research/3mkchc/the_tobacco?w=4%20%20ID:%204757741

13. Asian Pacific Journal of Cancer Prevention [Internet]. Journal.waocp.org. 2020 [cited 23 September 2020]. Available from: http://journal.waocp.org/

14. WHO report on the global tobacco epidemic 2011 [Internet]. World Health Organization. 2020 [cited 23 September 2020]. Available from: https://www.who.int/tobacco/global_report/2011/en/

15. Chadda R, Sengupta S. Tobacco use by Indian adolescents. Tobacco Induced Diseases. 2003;1(1):8.

16. Ray J, Smitha T. Oral submucous fibrosis: An update. Journal of Oral and Maxillofacial Pathology. 2017;21(3):330.

17. Torrens P. Growing Up Tobacco Free. JAMA: The Journal of the American Medical Association. 1995;273(17):1326.

18. Shukla I. A Prospective Observational Study on the Therapeutic Effect of Plantago Major in Reducing Craving for Tobacco. Homœopathic Links. 2019;32(03):145-151.

19. Youths I, Lynch B, Bonnie R. THE NATURE OF NICOTINE ADDICTION [Internet]. Ncbi.nlm.nih.gov. 2020 [cited 23 September 2020]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK236759/

20. Health Effects of Smoking and Tobacco Use [Internet]. Centers for Disease Control and Prevention. 2020 [cited 23 September 2020]. Available from: https://www.cdc.gov/tobacco/basic_information/health_effects/index.htm

21. Ambrose J, Barua R. The pathophysiology of cigarette smoking and cardiovascular disease. Journal of the American College of Cardiology. 2004;43(10):1731-1737.

22. WY C, GE P, AM J, JE H. Cigarette smoking-associated changes in blood lipid and lipoprotein levels in the 8- to 19-year-old age group: a meta-analysis [Internet]. PubMed. 2020 [cited 23 September 2020]. Available from: https://pubmed.ncbi.nlm.nih.gov/2136949/

23. Cobb C, Ward K, Maziak W, Shihadeh A, Eissenberg T. Waterpipe Tobacco Smoking: An Emerging Health Crisis in the United States. American Journal of Health Behavior. 2010;34(3):275-285.

24. Buchmann A, Blomeyer D, Jennen-Steinmetz C, Schmidt M, Esser G, Banaschewski T et al. Early smoking onset may promise initial pleasurable sensations and later addiction. Addiction Biology. 2011;18(6):947-954.

25. Wadgave U, L. N. Nicotine Replacement Therapy : An Overview. International Journal of Health Sciences. 2016;10(3):407-416.

26. Thomas K, Martin R, Davies N, Metcalfe C, Windmeijer F, Gunnell D. Smoking cessation treatment and risk of depression, suicide, and self harm in the Clinical Practice Research Datalink: prospective cohort study. BMJ. 2013;347(oct11 1):f5704-f5704.

27. (COVID-19) C, Health E, Disease H, Disease L, Management P, Conditions S et al. Nicotine Replacement Therapy: What to Know [Internet]. WebMD. 2020 [cited 23 September 2020]. Available from: https://www.webmd.com/smoking-cessation/nicotine-replacement-therapy

28. Lee P, Fariss M. A systematic review of possible serious adverse health effects of nicotine replacement therapy. Archives of Toxicology. 2016;91(4):1565-1594.

29. pharmacopoeia T. The American homoeopathic pharmacopoeia - Digital Collections - National Library of Medicine [Internet]. Collections.nlm.nih.gov. 2020 [cited 23 September 2020]. Available from: https://collections.nlm.nih.gov/catalog/nlm:nlmuid-101313392-bk

30. Caladium. - A DICTIONARY OF PRACTICAL MATERIA MEDICA By John Henry CLARKE, M.D. Presented byM&#xfffd;di-T &#xfffd;[Internet]. Homeoint.org. 2020 [cited 23 September 2020]. Available from: http://www.homeoint.org/clarke/c/calad.htm

31. CALADIUM. - THE ENCYCLOPEDIA OF PURE MATERIA MEDICA By TIMOTHY F. ALLEN, A.M., M.D. [Internet]. Homeoint.org. 2020 [cited 23 September 2020]. Available from: http://www.homeoint.org/allen/c/calad.htm

32. Caladium Seguinum. - THE GUIDING SYMPTOMS OF OUR MATERIA MEDICA By CONSTANTINE HERING, M.D. [Internet]. Homeoint.org. 2020 [cited 23 September 2020]. Available from: http://www.homeoint.org/hering/c/calad.htm