

# Clinical efficacy of herbal coded formulation Ocucure for the improvement of presbyopia: A randomized comparative clinical trial

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**Abstract:** A progressively diminishing capacity of eye to visualize for close proximity increasing by age is known as presbyopia which is usually resulted due to loss of elasticity of crystalline lens. A clinical trial was conducted to evaluate the efficacy of coded herbal formulation "ocucure" (Test drug) for the treatment of presbyopia comparing with leutivit (Placebo). One hundred and eleven patients suffering from presbyopia from both groups (Males: 63, mean age: 34±14 and females: 48, mean age: 33±13 year, range: 20-60) were enrolled in the trial and divided in to two groups according to treatment regimens. Ocucure (Test drug) 500mg two tablets and leutivit (Placebo) 250mg tablets twice daily were prescribed for 6-8 weeks. Presbyopia was improved in 17 patients (28.81%) out of 59 patients by the use of ocucure (Test drug), and in 6 patients (11.53%) out of 52 by the use of leutivit (Control drug). Furthermore, there was a significant improvement in presbyopic associated clinical features as compared to leutivit. It is concluded that ocucure possesses a therapeutic value for the improvement of presbyopia and its associated symptoms as compared to leutivit.

**Keywords:** Presbyopia, treatment, herbal drugs.

## INTRODUCTION

A progressively diminishing capacity of eye increasing by age to visualize for close proximity is known as presbyopia. The accurate mechanism of this disorder is still not known completely but there are some strong evidences from research studies that crystalline lens lost their elasticity (Murube *et al.*, 2001). Further studies demonstrated that ciliary muscles those are involved in the bending and straighten the lens loss their power resulting in continuous change in lens curvature is major cause of presbyopia (Malecaze *et al.*, 2001). Presbyopia is considered mainly due to aging, usually results between the ages of 40 and 50 which is eyestrain, problems such as see in dim light unable to focus small objects (Johannsdottir and Stelmach, 2001). The power to see near things in a childhood is about 20 dioptries which means to see the objects about 50 mm for way and at age 25 it is 10 dioptries (100 mm) but at age 60 this is 1 dioptries that result to focus 1 to 2 meters only (Berendschot *et al.*, 2002).

The patients suffering from presbyopia usually feel that a visual impairment is happening due to the gradual loss of near vision that may deprive the quality of their lives. In reality, the inevitable degradation of accommodative power in human visual systems starts in childhood and at the age of 50 everyone completely realizes its adverse effects (Westin *et al.*, 2000). In United States approximately more than 100 million people are affected by this degenerative problem over the age of 50 according

to 2010 U.S. Census which provides only a glimpse of the global influence of this ocular condition. Previously in 2005, it was estimated that 1.04 billion people worldwide are suffering from presbyopia, in which 410 million people were labeled as visually impaired due to lack of adequate near corrections. The increasing prevalence of this disorder is alarming and to explore the innovative surgical approaches are the need of time to manage this treatable condition (Li, 2006).

Presbyopia can be corrected by many ways by bifocal spectacles or mono-vision contact lenses and with refractive surgery. Vision centres are now providing the facilities of selling the glasses of +4.0 diopter or higher ranges of magnification lenses. In mono-vision method patient select contact lens to control one eye for near and one for far vision that can interfere with depth perception (Reinstein, 2009). Eye exercises also delay the onset of presbopia but itsproper efficacy is not determined by researchers. New surgical techniques are also providing a better management for those who want to get rid-off glasses or contact lens, including the implantation of accommodative intraocular lenses (IOLs). Scleral expansion bands, which expand the space between the ciliary body and lens, have not been found to provide good results. In many European countries INTRACOR technique has now been very popular for treatment of both eyes for reading glasses (Jain *et al.*, 1996). Cornea is reshaped by surgical treatments like PresbyLASIK and Conductive Keratoplasty but after surgical corrections little use of reading glasses will still be needed in dim light or when reading for prolong periods of time (Pallikaris *et al.*, 2003).

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There is a great need to find new medicinal agents which have good efficacy and less adverse effects for the management of presbyopia. Herbal medicine could be choice to treat presbyopia and relieving the clinical sign and symptoms. So considering this option, a formulation was designed based on literature citation. Previously it has been reported that many herbs possess potential to treat eye disorders e.g., *Foeniculum vulgare* and *Paeonia officinalis* roots have been reported having effects in the management of presbyopia (Guilled and Manzanons, 1996). Coded herbal formulation Ocucure was designed which contains *Foeniculum vulgare*, *Paeonia officinalis*, *Coriandrum sativum* and *Benincasa hispida*.

## PATIENTS AND METHODS

A randomized controlled, two-arm parallel group clinical trial was conducted to evaluate the efficacy of ocucure (Test drug) as compared to leutivit (Placebo). The therapeutic evaluations of these medicines were conducted on 111 clinically and microscopically diagnosed cases from both groups (Males: 63, mean age: 34±14 and females: 48, mean age: 33±13 year, range: 20-60) at Dr. Muslim Eye Care Hospital Karachi. All the patients selected for the study were thoroughly examined and clinical history was recorded in the prescribed proforma. The therapeutic evaluation of the drug was made on the basic improvement in the visual acuity and other associated clinical features at periodic intervals during the course of treatment. Patients (n=111) were randomly assigned to receive ocucure 500mg two tablets in comparison with leutivit 250mg tablets twice daily for 6-8 weeks.

### Ethical issues and clinical trial approval

Study was conducted under the rules of Ethical Committee (EC) of Shifa-Ul-Mulk Memorial Hospital, Faculty of Eastern Medicine, Hamdard University Karachi, Pakistan. Study design and protocols were presented to the board members of Ethical Committee (EC) and Board of Advance Studies and Research (BASR) for their clearance and permission before the start of clinical trial.

### Test drugs formulation

Herbal coded formulation of compound drugs designed according to herbal pharmacopoeia monographs of Unani medicine on scientific basis. Each 500mg tablet contains; *Foeniculum vulgare*: 150mg, *Paeonia officinalis*: 150mg, *Coriandrum sativum*: 100mg and *Benincasa hispida*: 100mg.

All the medicinal plant drugs that were selected for ocucure were purchased from the Jodia market Karachi. The details are as follows; *Foeniculum vulgare* seeds, *Paeonia officinalis* roots, *Coriandrum sativum* and *Benincasa hispida* seeds. All the plant drugs were identified and authenticated by Prof. Dr. Usman Ghani

Khan, Professor, Department of Basic Clinical Sciences, Faculty of Eastern Medicine, Hamdard University Karachi, Pakistan. These herbs were cleaned thoroughly and grinded to make powder form. It is passed through the sieve to obtain the fine powder. Then binding agent are added and passed through a single punch machine to get fine tablets.

## STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS, MS excel software and Fisher exact test was applied. All differences were considered statistically significant by generating a 'p-value' from test statistics. The significant result with 'p-value' less than 0.05 was considered as statistically significant.

## RESULTS

### Patient characteristics

Baseline characteristics of all patients are given in table 1.

**Table 1:** Baseline characteristics of all patients in both test and control groups.

Characteristic	Ocucure	Placebo	p value
Male	33	30	NS
Female	26	22	NS
Age (yr)			
Mean ± SD	34±14	33±13	NS
Range	20-60	20-60	NS
Occupation			
Government employee	22	25	NS
Industrialist	20	15	NS
Agriculturist	08	06	NS
Miscellaneous	09	06	NS
Tobacco smokers	28	30	NS
Alcohol	0	0	NS

### Visual acuity

It was noted that 17 patients (28.81%) out of 59 patients by the use of ocucure (Test drug) showed improvement in visual acuity whereas it was in 6 patients (11.53%) out of 52 by the use of leutivit (Control drug). Chi-Square Test was applied and p-value was calculated as 0.0342 indicating that there is significant difference between these two drugs (table 2 and fig. 1).

**Table 2:** Impaired near vision after treatment

Visual acuity	Test (Ocucure)	Control (Leutivit)	Total (n)	p value
Improved	17 (28.81%)	6 (11.53%)	23	
Not improved	42 (71.18%)	46 (88.46%)	88	
Total	59	52	111	0.0342

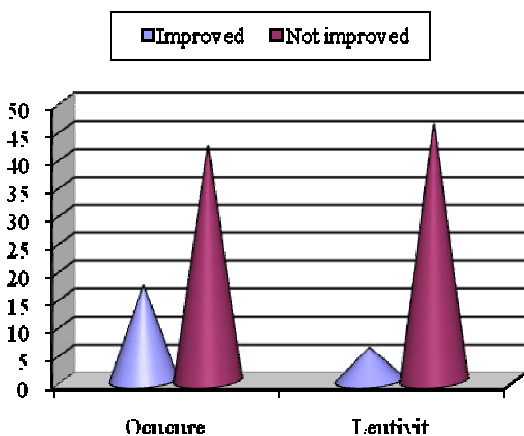


Fig. 1: Improvement in visual acuity by the use of Ocucure and Leutivit

Furthermore, improvement in clinical features associated with presbyopia such as near vision, headache, eye-ach, watering, blurring of vision and sinus problems were especially noted when treated with ocucure as compared to placebo (fig.2).

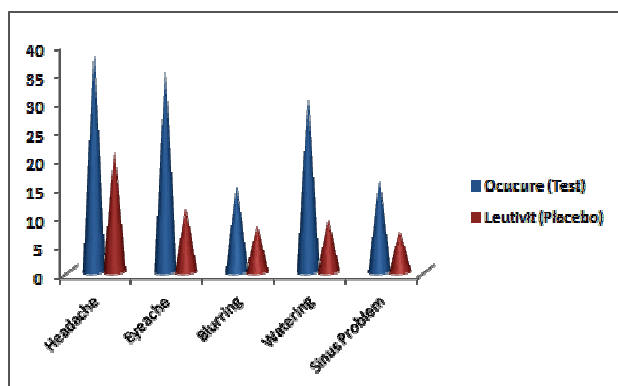


Fig. 2: Improvement in clinical features by both test and control groups.

## DISCUSSION

The most common clinical features of presbyopia are to read the fine print especially in dim light conditions, eyestrains in continuous reading for prolonged time period, blurring vision for distance objects and watering of eye (Robert, 2004). Measurement of visual acuity is the key diagnostic criteria to record the improvement in presbyopia (Cline et al., 1997). Patients suffering from presbyopia require an early treatment for both distance and close visions. Contact lenses are used commonly to relief this ailment. However there may be some other options to stop the development of this disease. Ocucure was formulated for this particular problem and found to be effective by this clinical trial. Reduction in the symptoms was noticed during the course of treatment by ocucure. The efficacy of herbal formulation is a characteristic of a complex mixture of chemical

compounds present in different herbs used as multiple dosage form design. Ocucure containing *Foeniculum vulgare* (fennel) which is aromatic herb of the Mediterranean region having tannic, gallic, caffeic, cinnamic, chlorogenic, ferulic and vanillic acids possessing therapeutic potential for treating various health disorders such as glaucoma, disorders of the central nervous system, hypertension, diabetes, skin infections and tuberculosis etc (Guilled and Manzanons, 1996). Coriander (*Coriandrum sativum*) contain tridecanoic acid, E-11- tetradecenoic acid, 2-decenoic acid. The seed oil contains linalool, acetic geranylo and a c-terpine has been used as herbal medicine for the treatment of anxiety, insomnia and other brain disorders (Carrubba et al., 2002; Sharma, 1996). *Paeonia officinalis* contains more than 262 compounds including Zonoterpenoid glycosides, flavonoids, tannins, stilbenes, steroids and triterpenoids, paeonols and phenols. It is commonly prescribed in vascular problems, headaches, epilepsy and stomach and menstrual disturbances (He et al., 2010). *Benincasa hispida* contains a small amount of protein, fat, fiber, carbohydrates, minerals, thiamin, riboflavin, niacin and vitamin C. These nutrients not only have important physiological activity, but also have many health effects in human body (Kumar et al., 2002).

Despite the broad use of herbal medicines, there is relative paucity of data available to demonstrate convincingly the safety and efficacy, and toxicity of these medicines to treat presbyopia and other eye disorders. The proposed herbal medicine will provide focal points for initiating, maintaining and to contribute to improved treatment and prevention of presbyopia. This will eventually lead to the development of evidence based herbal therapies for patients suffering from presbyopia.

## CONCLUSION

The finding from this clinical trial demonstrated the clinical assessment there was statistically significant difference when comparing the effectiveness of herbal medicine ocucure to leutivit (Placebo) for the treatment of presbyopia. Hence, ocucure possesses a therapeutic value for the treatment of presbyopia and its associated symptoms.

However, further clinical trials on larger scale and studies pertaining to mechanism of action of ocucure are required before prescribing it as an alternate therapy for presbyopia.

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