CSR Proposals of Social Relevance

1. Title of Project:

Decellularized corneal matrix hydrogel-based injectable hydrogel – a candidate for future treatment strategy for corneal indications

2. Background/Motivation:

We found that decellularized corneal matrix hydrogel (dCMH) has many advantages over existing materials, including easy availability, simple formulation procedures, biocompatibility, and preventing the trans-differentiation of corneal stromal keratocytes to myofibroblasts *in vitro,* which make it a promising material for corneal applications. We have prepared hydrogel from the bovine cornea and completed few preclinical studies to explore the potential of DCM hydrogel for corneal applications to check its feasibility to treat scar and corneal Ectasia. Ectasia has been classically described as a non-inflammatory pathology characterized by thinning of the cornea. The etiopathogenesis is still under research, and it may be the final manifestation of diverse pathologic processes. Keratoconus is considered the most common ectatic disorder of the cornea associated with corneal biomechanical instability. The existing treatment procedures are either risky or complicated surgical interventions are required. We demonstrated the efficacy of using dCMHs as a biomaterial to thicken the thinned ectatic cornea in an animal surgical model. It also provided information on the biocompatibility of dCMHs, its integration with native stroma, its degradation over time, and tissue remodeling. It would be a step towards developing a novel noninvasive technique for the treatment of corneal Ectasia by using decellularized extracellular matrix hydrogel.

3. Objectives of the project:

Since we have completed the preclinical study, the next step is to complete the toxicology study to proceed with human trials. A toxicology study will be essential to prove the safety of hydrogel during human applications.

1. Preparation and characterization of Cornea hydrogel from Bovine sources
2. Extensive Toxicology study
    a. Cytotoxicity Test
    b. Skin sensitization test
    c. Ocular Irritation in Rabbit
    d. Acute systemic toxicity test
    e Material Mediated Pyrogenicity
    f. Intraocular irritation in Rabbits – 3 days
    g. Intraocular irritation in Rabbits – 90 days
    h. Maximum dose ocular irritation and persistence in rabbits - 14 days
3. Data collection and documentation for Regulatory approval for human trial

4. Brief Methodology:

The hydrogel will be prepared as published (Chameettachal et al., 2020). Briefly, the bovine cornea will be collected from an authorized slaughterhouse and remove the cells by NaCl treatment. The decellularized tissue will be lyophilized and digest using enzymes. The prepared hydrogel will be tested in smaller animals s per ISO 10993-5, ISO 10993-10, ISO 10993-10, ISO 10993-11, ISO 10993-11 standards as a pre-requisite for human trials

5. Target population/Beneficiaries:

Impaired vision or blindness can affect a person's independence, education, employment, socioeconomic status, and mental health. We believe it is essential to take this problem as a challenge to overcome the high cost and lack of available human cadaveric cornea to treat the progressive ectatic corneal disorder. Blindness due to corneal disease is the fourth leading cause of global blindness and the second most frequent cause of blindness in developing nations. Globally, Keratoconus affects a preponderance of Indians, Pakistanis, Arabs, and Polynesians compared with Caucasian populations. Population studies have repeatedly found that Indians and Pakistanis make up a significantly greater percentage of patients with Keratoconus, suggesting a genetic component to the disease. The estimated incidence among Caucasians is 50/100,000. Regionally the mean age of onset is younger in Asian (18–24 years old) patients than in white patients (23–26 years old). The rate of progression is generally more severe in Asian keratoconus patients. So, if we can establish this new treatment strategy in India, it will be more beneficial for Indians and globally. Our research progresses by using bovine cornea, which is available abundantly, and low cost for formulating the hydrogel and requiring less skill to perform the procedure in clinics. Altogether, our technology is very relevant, with less Man, Money, and Material, and targeted a large community globally, particularly in India.

6. Expected Outcome/Deliverables:

1. A step forward to replacement for risky surgical interventions like bowman's membrane transplantation and other surgical procedures in practice for advanced Keratoconus and other patients with a less invasive procedure.
2. Development of novel injectable cornea tissue hydrogel for the clinical trial and to the global market in the future, which can be supplied cost-effectively.

7. Timeline and Budget: We consider the objectives as milestones, and the timeline is as follows.

	Year 1	Year 2	Year3
Budget (in Rs lakhs)	15.00	10.0	5.0
Milestones	Preparation and characterization of Cornea hydrogel from Bovine sources	Extensive Toxicology study	Data collection and documentation for Regulatory approval for human trial

8. Proposer Name & Designation:

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