**PROPOSAL**

**TITLE: Novel Cost Effective Cholic acid Based Clinical Intervention For Septicemia**

1. **Personal Information**

Name: Dr. Manu Saini

Qualification Ph.D

Designation Post Doctoral Fellow

Department (if student)

Year of passing (if alumni)

Designation (if faculty)

Address CEPIN Department, Institute of Nuclear Medicine and Allied Sciences, Brig. S.K. Mazumdar Marg, Lucknow Road, Timar Pur, New Delhi-10088

Date of Birth 19/12/1985

Gender Female

Tel, mob, fax, email 9999779365

Collaborating Inst / industry, if any DRDO

1. **Abstract/Summary of the Proposal**

Septicemia is defined as the blood stream infection, also known as bacteremia or blood posioning. Septecimia occurs when a bacterial infection elsewhere in the body, such as skin enters the blood. Treatment of septicemia is one of the major challenge in the healthcare industry as it can become life threatning if left untreated. The accumulation of bacterial species at the site of infection is the major cause of septicemia. The aggregated bacteria forms a biofilm at the site of wound/infection. Biofilms are surface-attached bacterial communities encased in a matrix of exopolysaccharides, proteins, and extracellular DNA. Biofilm-embedded cells are highly resistant to antimicrobials and disinfectants and therefore are difficult to eradicate. It has been shown that at least half of all chronic wounds contain biofilm, which delays the wound healing and the implications of which are considerable. It has been estimated that biofilm formation contributes topersistence and virulence of up to 80% of microbial infections in the human body and of many hospital-acquired infections, particularly in cases when in-dwelling medical devices are required. Many bacterial species colonize in-dwelling catheters as biofilms, inducing complications in patients' care. All types of catheter are vulnerable to encrustation by these biofilms, and clinical prevention strategies are clearly needed, as bacteria growing in the biofilm mode are resistant to antibiotics. Biofilms have great importance for publichealth because of their role in certain infectious diseases and importance in a varietyof medical device-related infections. Therefore, there is an urgent need to develop novel, effective and specific anti-microbial agent, which can be utilized to diminish the biofilm associated pathogenicity in hospital and other public spaces.

It is proposed to use bile acids, particulary; cholates/cholic acid in detachment/removal of biofilm from the site of infection (wounds) and from in-dwelling medical devices, thereby, reducing the septicemia.

The following bile acid products are proposed to be manufactured and commercialized through this start-up:

Under medical license

1. Bile acid based ointment for wound healing and biofilm disruption
2. Bile acid based Injectables

**C. Introduction to Ideation**

* 1. Broad Industry Sector:

Healthcare

* 1. What is the Product/Service

Bile acids containing ointment/injectable that can act as agent to remove bacterial biofilms from wounds leading to attenuation of septicemia.

* 1. Who is recepient/ beneficiary of your Product/Service?
* Patients in hospitals and other public spaces
* Medical and healthcare industry
  1. What is the idea/innovation
* Biofilm formation leads to septicemia instances at wound site due to
  + Aggregation of bacterial species
  + Antiobiotic/disinfectant resistance
  + Increased microbial infection delaying wound healing process
* Bile acids being natural surfactant, amphipathic nature and presence of a steroid nucleus in their structure can be potent anti-biofilm agent.
  + Significantly lower biofilm formation reducing the cost of infection treatment and decreased cases of septicemia
  + More cost reduction because clinical intervention cost comes down.

4a. Is it an Idea or you have validated any proof of concept?

* It is an idea, however preliminary laboratory studies proves bile salt as a potent antimicrobial agent.

4b. If you have started any work on it, has it generated some revenue?

No.

* 1. What experiments will you like to do
     1. Lab experiments to quantify biofilm
     2. in-vitro and in-vivo test to show biofilm formation and its removal through formulation comprised of bile salt.
     3. Lab experiment to study wound healing
     4. Clinical studies of formulations
  2. What will be requirement to get idea conceptualized
     1. Funds
     2. Tie up with the hospitals and health industry for scale up experiments & batch manufacture
     3. Understanding the local License procedures for smoother execution
     4. Administrative module with defined role of incubator & mentors. Internal financial & administrative rule book/SOP
     5. Market survey (brief)
     6. Back up exit plan: ToT of the technology to a bigger player

1. **Startup Plan**
   1. Who are the targeted founders/co-founders/promoters
      1. The core team consists of 04 young entrepreneur lead by Dr Manu Saini. Bio data of the founder member is attached.
   2. Specify role of each promoter/mentor

There are 02 mentors:

* Dr. Aseem Bhatnagar, (Sc ‘G’ & Additional Director, INMAS DRDO): 30 yrs experience in device innovations and implementation.
* Prof. Ruchika Kube, Medical Doctor, School of Health Sciences, IGNOU.

Dr Assem Bhatnagar will be providing technical and scientific mentoring.

Dr Kube shall help with dispute resolution and documentation.

We intend to produce the products ourselves in the first year. Thereafter, depending upon the demand, more machines will be purchased or

Since how long have you been working together on this idea

* 3 years. Feasibility discussion was done with INMAS doctors. Clinical trials conceived at INMAS, done outside.

1. **On Your Business Idea**
2. What is the financial viability plan for start-up

* All the bile salts based products have a large catchment market and not much competition.
* There is a perceived need. This is a high divident low investment ides
* All advantages accruing to start-ups will be incorporated and all responsibilities executed as per Law.
* Company SOP will be created as an official document.
* Provision of shared patents with incubator & user agencies (who contribute by way of trials and for specifications fine tuning) will be a stated policy of the company.
* Seed money need estimate: Rs 20 L
* Operations from home for 02 yrs to cut down expenses. Official address may also be provided by the incubator: DIIF
* No expenses on food / class 4 employees from the seed fund. Expenditure from fund on travel will be severely restricted, and will be as per SOP. Advertisement will be done through personal and social network with a small budget on brochures etc.
* Specifications will be sealed with participation of User agencies. Demand shall be generated on paper to the extent possible prior to the production.
* Rs 12 lakhs expenditure expected in the first 18 months on industrial prototyping, trials, licensing and production. Rs 08lakhs will be kept as reserve for ‘May Day’.
* Return on investment expected at the end of 04 month period.
* Break even expected at 15 months period.
* Continuation of the start-up or ToT to a bigger company will be a consensus decision at the end of 24 month period.

1. What are the sources of funds from self / other cofounders / anticipated from the incubation centre
   * 1. Team leader: Rs. 1 L
     2. Other cofounders: Rs 1 lakhs from 4 other cofounders.
     3. Rs. 20 lakhs from incubator.

1. Anticipated competition and current industry position with respect to your idea
   * 1. No similar products in Indian market.
2. Uniqueness of your start-up with respect to the product /service

* Only we are privy to the technology (apart from DRDO) as we conceived it.
* Team members have themselves worked on the concept and the products academically.
* Members have participated in clinical trials and product formulation discussions
* Team has young members, but they already have start-up experience. Mentors have more than 06 decades of cumulative experience covering all areas where mentorship will be needed.
* Team members have complimentary abilities that cover Science & technology, Product development, management & administration experience.
* Team members know each other for more than 3 years, and association with mentors is > 06 months old.
* Product idea has matured and some clinical trials have already been done suggesting seriousness of approach.
* ‘Make in India’ approach

1. How do you view your technology / idea with respect to sustainability

* Products are niche, innovative, relevant & cost effective. These are not ‘Me Too’ products.
* There is a very big market to be tapped.
* There appears to be significant ‘need’ and societal benefit
* Technology is quite simple with practically no failure issue. The only issue is acceptability and our power to convince
* Industry partners / mentors already in loop.
* Infusion of our own funds and bank loans will ensure that the team will put all efforts towards success of the venture.
* Feasibility worked out in terms of
  + Efficacy & safety
  + Cost
  + Market potential
  + Local infrastructure & licensing position
  + Fund management
  + Government market / defence market (through DRDO MOU)

1. Target Market (customer segment) identification; market size and trend, how much market share you can gain over next 03 years

* Medical industry
* Health care industry
* Hospitals & nursing homes
* Medical shops whole salers
* we expect the following market upfront at the end of 1st year &3 yrs:

|  |  |  |
| --- | --- | --- |
| Item | 1styr | 3rdYr |
| 02 therapeutic products | 20000 units | 10 lakhs units |

1. **Strategy**
2. What if you do not get the incubation support from DIIF

* The project will be delayed by 06 months for want of returnable funds
* We shall have to loom for similar incubators
* The team leader will be under stress to keep the flock together for 6 months.
* Market will have to wait for 06 potential utility/medical items for 06 months despite need & felt demand

1. What if you get the incubation support from DIIF
   * 1. The above stated process will be kick-started immediately.
     2. We shall apply for loans from banks/put in our funds to initiate the process immediately
     3. Administrative work to initiate start-up and technical work for pre-production shall be initiated immediately, even ahead of actual funding, on the basis of written commitment from the incubator
     4. We shall have a meeting with incubator mentors immediately to make a work plan by consensus.
2. How do you plan to scale up your start-up

* Initially job contract to relevant units already existing
* Later on, we may share equity with other companies to install more machines or invest more funds on personal account or expand Directors number.
* As part of Plan B for manufacture, 1-2 standby sites will be kept in loop so that smooth substitution can be done in case things do not work out with the original site.
* With time, a manufacturing facility may be created.

1. What are the challenges you are facing now and you foresee in the next 2 years

* Acceptability of new product is always a slow process
* Inter-phasing with similar but not-so-effective products will be a bigchallenge.
* Business and incubation opportunities are limited in reality inspite of efforts being made by various organs of the government.
* The rule book is too heavy for new start-ups who are fresh and need to concentrate on technology maturation rather than hurly and burly of running to govt depts. for approvals.
* Start-ups, particularly those funded by government, today face a bad name and credulity issue because of high failure rate &failure to return the investment. To convince VCs that our start-upeffort is genuine and approach balanced and technically sound is a challenge.
* Detailed Market survey not done because of cost and complexity involved.

1. **Requirements**
2. Infrastructure required

* Office space now and then. Operations shall be done from home initially and meetings will be positioned at fabricator establishments since these are formal mature agencies.
  + - 1. Justification: a) Allowed as per Incubator concept note, b) Upfront/hire charges can be managed from the seed fund as per rules/norms.

1. Requirement of the meeting room (frequency of meeting / month)

Not needed

1. Incubator Funds required upto 2 years

Maximum 02 instalments within the first 09 months. Justification: major expenses are in the initial phase only

1. Incubator & mentor assistance required upto 02 years.
2. **Expected Milestones (every 06 months)**
   1. Submission of SOP of company to incubator cell within 01 months of approval.
   2. Submission of letters of demand /letter of Intent from Users (dealers) and MOU with feeder industries within 01 months of sanction letter.
   3. Industrial prototype and demo of functionality of clinical interventions in 06 months.
   4. Industrial production: 06 months.
   5. User appraisals/trials & modification (Mark-2) : 12 months
   6. Production of Mark-2 formulations in desired numbers: 18 months
   7. Ploughing back of funds for perpetual production: 15-21 months.
   8. Report preparation and maturation of start-up function: 21-24 months.

**RESUME**

**MANU SAINI, PhD**

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**CAREER OBJECTIVE:**

Looking for the employment opportunity where I can use my skills and knowledge in the field of healthcare, drug development and biotechnology.

**EDUCATIONAL QUALIFICATION:**

|  |  |  |  |
| --- | --- | --- | --- |
| **Exam Passed** | **Board/University/Deptt.** | **Subjects** | **Division** |
| Ph.D | Jamia Hamdard, Delhi | Biotechnology  Thesis title “Radioprotection Studies with Herbal Preparation” | First |
| M.Sc (2008) | Punjab Technical University, Jalandhar | Biotechnology | First |
| B.Sc (2006) | Delhi University | Botany (Honors) | First |
| XIIth (2003) | CBSE | Physics, Chemistry, Biology | First |
| Xth (2001) | CBSE | All Compulsory | First |

**PRESENT POSITION:**

* Working as a National Post-Doctoral Fellow (Science and Engineering Research Board, Department of Science and Technology, Govt. of India) at Institute of Nuclear Medicine and Allied Sciences (INMAS), DRDO, New Delhi, India.

**RESEARCH EXPERIENCE:**

* I am having practical experience in identification and quantification of phytochemicals, irradiation of animals with 60Co-gamma and UV-rays; biochemical assays for studying antioxidant status and markers of oxidative stress, histology, histochemistry, immunomodulation, protein expression and gene expression changes. Such an experience was gained while performing work towards compilation of PhD thesis and the work was performed at Institute of Nuclear Medicine and Allied Sciences (INMAS), DRDO and Jamia Hamdard, New Delhi, India.
* **Dissertation project** entitled “**Some in vitro and in vivo Studies with Hippophae rhamnoides**” for six months was completed at Institute of Nuclear Medicine and Allied Sciences, Department of Radiation Biology, New Delhi, India in which binding of ds-mouse genomic DNA and on ss-synthetic DNA, rich in GC sequences with herbal drugs was studied using spectrophotometer assays.
* **Summer training** for one month was completed atAll India Institute of Medical Sciences, Department of Forensic Medicine and Toxicology,New Delhi, India in which DNA/RNA isolation, quantification and purification of DNA/RNA isolated from blood sample and tissue sections was performed.

**TECHNICAL SKILLS:**

* **Animal Handling:** Handling, feeding and dissection of experimental mice and rat.
* **Analytical Methods with Herbs/Botanicals:** Soxhlet extraction, Lyophilization, HPTLC
* **Molecular Biology Techniques:** DNA/RNA isolation, quantification and purification from blood sample and tissue sections; Real Time Q-PCR; Laser Micro-dissection, Micronuclei analyses etc.
* **Biochemistry:** Immunofluorescence, Western Blotting, PAGE, ELISA, Electrophoresis, Enzymatic assays.
* **Computer Skills:** MS-Word, Excel, Power-point

**PUBLICATIONS IN PEER REVIEWED INTERNATIONAL JOURNALS:**

* Madhu Bala, Manish Gupta, **Manu Saini**, M. Z. Abdin, and Jagdish Prasad (2015). Sea Buckthorn Leaf Extract Protects Jejunum and Bone Marrow of 60Cobalt-Gamma-Irradiated Mice by Regulating Apoptosis and Tissue Regeneration. Evidence-Based Complementary and Alternative Medicine, Volume 2015, Article ID 765705.
* **Manu Saini**, Madhu Bala, Humaira Farooqi, MZ Abdin, Jagdish Prasad (2014). Renoprotective activity of Hippopahe leaf extract in total body 60Co-gamma-irradiated mice: An oxidative and histopathology study. Int J Pharm Pharm Sci, 3, 161-166.
* **Manu Saini,** Athar Ali Khan, Madhu Bala, M.Z. Abdin, Humaira Farooqi(2014).Development of a validated HPTLC method for quantification of esculin in different fractions of Cichorium intybus leaf extract. Int J Pharm Pharm Sci, 6, 278-282.
* M Saifi, A Ali, **M Saini**, N Nasrullah, S Khan, MZ Abdin (2014). A rapid and efficient high-performance thin-layer chromatographic (HPTLC) method for simultaneous analysis of stevioside and rebaudioside-a in Stevia rebaudiana. Int J Pharm Pharm Sci,6, 455.464.
* Madhu Bala and **Manu Saini** (2013). Validated HPTLC Methods for Quantification of Marker Compounds in Aqueous Extract of Hippophae rhamnoides Leaves. In J Pharm Sci Rev Res, 23, 58-63
* **Saini M**, Tiwari S, Prasad J, Singh S, Kumar M S Y and Bala M (2010). Hippophae Leaf Extract Concentration Regulates Antioxidant and Pro-oxidant Effects on DNA. [Journal of Dietary Supplements](http://informahealthcare.com/loi/jds); **7**(1), 60-70.

**AWARDS:**

* **M R Raju Award** in International Conference on Radiation Biology “High LET Radiation Biology and Complex Natural Products in Biology & Medicine”, November 09-11, 2016, Chennai, India.
* **Young Scientist Award** in **“**International Conference of Radiation Biology”, November 11-13, 2014, New Delhi, India.
* **Oral presentation award** in National Conference on “Effectof Radiation on Human Race: Precautionary in Future”, March 1-2, 2013, Sri Ganganagar, India.

**PRESENTATIONS IN CONFERENCES/WORKSHOP/SEMINARS:**

* **Manu Saini**, Madhu Bala, Humaira Farooqi, MZ Abdin, Jagdish Prasad (2016). Gallic acid, quercetin, and rutin rich extract from leaves of Hippophae rhamnoides (SBL-1) counters 60Co-gamma radiation induced oxidative stress, changes in TNF-alpha, NGAL, cystatin C and FTL-1 in mouse kidney- Implications in radiation protection. **International Conference on Radiation Biology “High LET Radiation Biology and Complex Natural Products in Biology & Medicine”**, November 09-11, 2016, SRM University, Chennai, India.
* **Manu Saini**, Madhu Bala, Humaira Farooqi, MZ Abdin, Jagdish Prasad (2015). Hippophae rhmanoides leaves extract counters 60Co-gamma radiation induced oxidative stress, inflammation and changes in m-RNA level in mouse kidney. **National Conference on Herbal Medicines: Current strategies and future prospects”**, December 22-24, 2015, University of Rajasthan, Jaipur, India.
* **Manu Saini**, Madhu Bala, Humaira Farooqi, MZ Abdin, Jagdish Prasad (2014). Seabuckthorn leaf extracts (SBL-1) counters radiation induced renal histopathology, oxidative stress as well as mRNA levels. **International Conference on Radiation Biology Frontiers in Radiobiology: Immunomodulation, Countermeasures & Therapeutics”**,November 11-13, 2014, National Agriculture Science Complex, Pusa Road, New Delhi, India.
* **Manu Saini**, Madhu Bala, Humaira Farooqi, MZ Abdin, Jagdish Prasad (2014). Hippophae rhmanoides render renoprotection to 60Co-gamma irradiated mice by neutralizing oxidative stress. **“National Seminar on Plant Biotechnology: Challenges and opportunities in 21st Century”**,March 03-04, 2014, Jamia Hamdard, New Delhi, India.
* Manu Saini and Madhu Bala (2013). Quantification of antioxidant 3,4,5-trihydroxybenzoic acid in radioprotective drug SBL-1 and its modifying effects on radiation induced changes in renal oxidative stress. **“International Conference on Radiation Biology & Clinical Applications: A Molecular Approach towards Innovations in Applied Radiobiology”**, October 25-27, 2013, Mangalore, India.
* Manu Saini, Jagdish Prasad, Madhu Bala. Hippophae leaves reduces radiation induced lipid per-oxidation and renal pathology in total body 60Co-gamma- irradiated mice. National Conference on “**Effect of Radiation on Human Race: Precautionary in Future”,** March 1-2, 2013, Sri Ganganagar, India.
* Manu Saini, Jagdish Prasad and Madhu Bala. Protective role of Hippophae leaves against kidney damage in total body 60Co-gamma irradiated mice. International Conference on “**Emerging Frontiers & Challenges in Radiation Biology**”, January 24-25, 2012, Bikaner, India.
* Saini M, Prasad J, Singh S, Bala M (2010). Hippophae leaves protect bone marrow in whole body 60Co gamma-irradiated mice. International Conference on “**Radiation Biology-** **Nanotechnology, Imaging and Stem Cell Research in Radiation Oncology (ICRB-NISRRO)**”, November 15-17, 2010, Chennai, India.
* Saini M, Tiwari S, Prasad J, Singh S, Bala M. Hippophae leaf extracts and DNA interaction studies: implication in radioprotection. International Conference on “**Radiation Biology &Translational Research in Radiation Oncology**”, November 10-12, 2008, Jaipur, India.

**FELLOWSHIP:**

* **National Post Doctoral fellowship** (NPDF, SERB) awarded for a period of 2 years against project entitled **Study on “ETOSIS” and its regulatory molecular mechanisms in radiation injury.**
* **Senior Research Fellowship** (SRF, ICMR) awarded for a period of 3.5 years (26th March, 2013- 25th Sep, 2016) against project entitled “**Studies in murine model on radiation induced genetic, histopathological and biochemical changes in kidney and the protective effects of herbal preparation from Hippophae rhamnoide**s”.

**MEMBERSHIP PROFESSIONAL BODIES:**

* Life member of Indian Society for Radiation Biology.

**REFERENCES**

* Prof M.Z. Abdin

Head, Department of Biotechnology, Jamia Hamdard, New Delhi-10062.

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Director, Defence Institute of Bio-Energy Research (DIBER), Haldwani, District- Nainital (Uttarakhand)

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**DELCLERATION:**

I hereby declare that above mentioned information is true to best of my knowledge.

**MANU SAINI**