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Development of triphala churna extract mediated iron oxide nanoparticles as novel treatment strategy for triple negative breast cancer

Ankita Parmanik [a], Anindya Bose [a,*], Bhavna Ghosh [a,b], Milan Paul [c], Asif Itoo [c], Swati Biswas [c], Manoranjan Arakha [d]

[a] School of Pharmaceutical Sciences, Siksha O Anusandhan (Deemed to be University), Bhubaneswar, Odisha, 751003, India
[b] Sri Jayadev College of Pharmaceutical Sciences, Naharkanta, Via: Balianta, Bhubaneswar, Odisha, 752101, India
[c] Department of Pharmacy, Birla Institute of Technology & Science-Pilani, Hyderabad Campus, Jawahar Nagar, Kapra Mandal, Medchal District, Telangana, 500 078, India
[d] Center for Biotechnology, Siksha O Anusandhan (Deemed to be University), Bhubaneswar, Odisha, 751003, India

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ABSTRACT

The present work demonstrates the eco-friendly green synthesis of Iron oxide nanoparticles from the aqueous extract of Triphala churna (TIONPs) using ferric chloride hexahydrate ($FeCl_3.6H_2O$) precursor in a single-step process. The formulated TIONPs were characterized by various instrumental techniques such as UV–Visible spectrophotometry (UV–Vis), Atomic absorption spectroscopy (AAS), Fourier transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD), Scanning electron microscope (SEM), Dynamic light scattering- Zeta potential (DLS-Zeta sizer), and Superconducting quantum interference device (SQUID) to establish their physico-chemical characteristics. The average size range of obtained spherical TIONPs was found in between 29 and 74 nm. Further, the MTT assay and Nuclear staining assay were carried out on Triple negative breast cancer (TNBC) cell lines along with a breast cancer associated epidermoid skin carcinoma cell line. The MTT assay revealed prominent cytotoxic activity of TIONPs against the tested cancer cell lines. Additionally, the nuclear staining assay revealed that the cytotoxic activity of these nanoparticles occurred via apoptosis mode by exhibiting nuclear fragmentation, cytoplasmic shrinkage, and cell blebbing. These TIONPs were also found to possess superparamagnetic property which may be additionally beneficial for their rapid and organ targeted delivery. Hence, the green synthesized TIONPs can be explored in near future as a new promising option for TNBC management.

1. Introduction

Cancer is considered as a significant cause of death worldwide. The initiation of cancer is very fast and can rapidly spread to the other healthy cells and tissues of the body. Among various cancers, breast cancer is considered as the second most cause of death globally. Breast cancer accounts for about 14% of cancer in Indian women. A report on breast cancer statistics has confirmed that the new breast cancer cases had risen to 1,62,468 in 2018, and the death rate was estimated as 87,090 [1]. Conventional chemotherapeutic drugs experience some limitations in distinguishing between normal and cancerous cells, leading to systemic toxicity and severe side effects [2].

Triple-Negative Breast Cancer (TNBC) is a type of breast cancer that is aggressive and prone to rapid multiplication at the lymph nodes and has a higher chance of recurrence [3]. Once cancer spreads to the lymph nodes or other parts of the body the chances of survival rate of a patient is greatly reduced. It has been reported that the TNBC can grow very faster and eventually spread to a great extent at the time of its diagnosis [4]. As the three prominent women's hormonal receptors (Progesterone, Estrogen and Human epidermal growth factor) are not present in TNBC, hormone therapy or immunotherapy are excluded from the list of treatments for TNBC. Hence chemotherapy using taxanes, anthracyclins, PARP inhibitors, etc. remains the major treatment against TNBC. Unfortunately, inherited cytotoxic activity, non-targeted delivery, and higher doses of these chemotherapeutic drugs result in severe systemic side effects and poor prognosis and the destruction of a large number of healthy cells compared to the TNBC cells. Therefore, it is the high time to implement advanced and novel strategies like nanotechnology in the

* Corresponding author.
E-mail address: anindyabose_in@yahoo.com (A. Bose).

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Review article

Targeted anticancer drug delivery via surface engineered iron oxide nanoparticles: A recent update

Ankita Parmanik, Anindya Bose *

Department of Pharmaceutical Analysis, School of Pharmaceutical Sciences, Siksha 'O' Anusandhan (Deemed to be University), Khandagiri, Bhubaneswar, Odisha, 751003, India

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ABSTRACT

Cancer treatment is a challenging task due to the complexity and variation of the disease, late diagnosis, and severe side effects of the antineoplastic agents. Targeted drug delivery via surface-engineered iron oxide nanoparticles (IONPs) can improve treatment effectiveness while reducing the severity of adverse effects. The effective size control capabilities and superparamagnetic behavior make IONPs a promising drug delivery system for cancer treatment. Their preparation methodologies should optimize essential attributes like size, shape, and superparamagnetic properties. Furthermore, their surface properties must enhance colloidal stability and half-life in the bloodstream. This review describes various surface coating agents currently employed to stabilize the IONPs and their recent uses in targeted drug administration. Surface modified IONPs can be cross-linked with tumor-targeting ligands (like monoclonal antibodies, peptides, and proteins) for their delivery to the cancer-targeted site with/without utilizing their magnetic properties. Their active targeting approach can reduce the dosage requirement for efficient drug binding. On the contrary, the passive delivery of IONPs is influenced by their physicochemical properties and particle size. Surface modification with biopolymers can minimize blood protein opsonization, extending blood circulation and sustaining drug release at the cancer site. On the other hand, metal and metal oxide are employed as doping agents on the surface of IONPs to provide good physical and biological strength. Surface functionalized IONPs may become the next generation cancer treatment strategy; however, more study into their clinical applicability and commercialization is required.

1. Introduction

Cancer remains one of the most heart-throbbing causes of death nowadays. According to National Centre for Health Statistics data, 1,958,310 new cancer cases are expected in 2023, with around 609,820 cancer deaths globally. As per the projections, there will be 30 million new instances of cancer worldwide by 2040, mostly in low- and middle-income nations. The cancer statistics are expected to rise by 60% within two to three decades [1]. In particular, India has a low survival rate of 66.1% for women diagnosed with breast cancer compared to other countries [2]. The fundamental reason behind the lower success rate for cancer treatment is the social awareness about cancer, high-cost treatment, side effects due to chemo-radiotherapy, and issues like delayed detection [3]. Techniques like imaging of tissue samples, unavailability of effective biomarkers for cancer diagnosis and prognosis, and surgical exploration tried by doctors often catch cancer too late to achieve a cure [4].

It is a well-accepted fact that the side effects of drugs are mostly related to their non-specific action. The current chemotherapeutics have significant trouble differentiating between healthy cells and malignant cells, which can cause systemic toxicity and produce serious treatment resistance, which refers to multi-drug resistance (MDR) [5].

Conventional chemotherapeutic drugs take much time to reach the target site to display their action, which may lead to severe systemic side effects by disturbing the normal cells. Additionally, the broad-spectrum anticancer agents have slow bio-distribution, which may lead to blockage in the targeted site. These factors limit the use of chemotherapeutic medicines in cancer treatment. In many cases, the severe side effects of traditional anticancer medications necessitate therapy discontinuation as the sole option [6].

"Nano-oncology," a branch of nano-biotechnology with a very narrow emphasis, is gaining popularity nowadays to overcome many of the limitations of conventional chemotherapeutic agents [7]. In such cases, iron oxide nanoparticles can be used to improve cancer detection and

* Corresponding author. School of Pharmaceutical Sciences, Siksha O Anusandhan (Deemed to be University) Bhubaneswar, Odisha, 700015, India.
E-mail addresses: anindyabose_in@yahoo.com, anindyabose@soa.ac.in (A. Bose).

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REVIEW ARTICLE

Current Treatment Strategies Against Multidrug-Resistant Bacteria: A Review

Ankita Parmanik[1] · Soumyajit Das[1] · Biswakanth Kar[1] · Anindya Bose[1] · Gaurav Raj Dwivedi[2] · Murali Monohar Pandey[3]

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Abstract

There are several bacteria called superbugs that are resistant to multiple antibiotics which can be life threatening specially for critically ill and hospitalized patients. This article provides up-to-date treatment strategies employed against some major superbugs, like methicillin-resistant *Staphylococcus aureus*, carbapenem-resistant *Enterobacteriaceae*, vancomycin-resistant *Enterococcus*, multidrug-resistant *Pseudomonas aeruginosa*, and multidrug-resistant *Escherichia coli*. The pathogen-directed therapeutics decrease the toxicity of bacteria by altering their virulence factors by specific processes. On the other hand, the host-directed therapeutics limits these superbugs by modulating immune cells, enhancing host cell functions, and modifying disease pathology. Several new antibiotics against the global priority superbugs are coming to the market or are in the clinical development phase. Medicinal plants possessing potent secondary metabolites can play a key role in the treatment against these superbugs. Nanotechnology has also emerged as a promising option for combatting them. There is urgent need to continuously figure out the best possible treatment strategy against these superbugs as resistance can also be developed against the new and upcoming antibiotics in future. Rational use of antibiotics and maintenance of proper hygiene must be practiced among patients.

Introduction

Antimicrobial resistance is the capability of a microorganism to resist the action of the different antimicrobials. In this type of resistance, microbes can resist the medication that could once be successful against them [1]. When this resistance occurs to multiple drugs, it is known as multidrug resistance (MDR). There are different types of resistance mechanisms observed in microbes, like natural resistance in certain microbes against a particular antimicrobial, genetic mutation, or acquired resistance from other species [2].

Globally, the drug resistance is increasing due to indiscriminate use of antimicrobial agents. Resistance microbes are hard to treat, requiring alternative or higher doses of antimicrobials or lack/shortage of effective antimicrobials, adversely affecting countries at all levels of development. As per the statement of World Health Organization (WHO), MDR pathogens called 'superbugs' are one of the major public threats that yearly cause several million deaths globally [3]. In 2021, WHO published the list of antibiotic-resistant pathogens (priority pathogens), especially highlighting the resistant gram-negative bacteria that pose maximum threat to human health [4]. On the basis of urgency for new antibiotics, the list is categorized into three headings, mainly critical, high, and medium priority. The critical group of MDR bacteria includes *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Enterobacteriaceae*, which cause severe infections like pneumonia and blood stream infections in hospital-admitted patients. The high and medium priority group include drug-resistant bacteria like *Salmonella* that causes common diseases, such as gonorrhoea and food poisoning.

Many review articles have been published about multidrug-resistant bacteria and treatment strategies employed to combat them. However, most of these articles focus on a particular resistant bacteria or a specific line of treatment

✉ Anindya Bose
anindyabose_in@yahoo.com

[1] School of Pharmaceutical Sciences, Siksha O Anusandhan (Deemed to be University), Bhubaneswar, Odisha 751003, India

[2] ICMR-Regional Medical Research Centre, Gorakhpur, Uttar Pradesh 273013, India

[3] Birla Institute of Technology and Science (BITS), Pilani, Rajasthan 333031, India

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REVIEW

Research advancement on magnetic iron oxide nanoparticles and their potential biomedical applications

Ankita PARMANIK, Anindya BOSE *, Bhavna GHOSH

Department of Pharmaceutical Analysis, School of Pharmaceutical Sciences, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar, India

*Corresponding author: Anindya Bose, School of Pharmaceutical Sciences, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar, India.
E-mail: anindyabose_in@yahoo.com

ABSTRACT

Magnetic iron oxide nanoparticles (MIONPs) have turned into a big research hotspot in biomedical fields mostly due to their large surface area to volume ratio and inherent superparamagnetism property. Various physical and chemical methods have been developed for their synthesis such as coprecipitation, solvothermal reduction, thermal decomposition, electrochemical synthesis, etc. Although most of these methods suffer from operational hurdles as well as environmental hazards. Therefore research focus is now concentrating towards their synthesis from various biological or green resources like plant extracts, micro-organisms, algae, glucose, starch, clays, etc. Plant extracts are mostly acceptable for such type of green synthesis due to their ability to reduce iron ions rapidly as well as their easy availability in wide varieties. Magnetic iron oxide nanoparticles have been applied in various biomedical fields such as targeted localization, magnetic hyperthermia, magnetic resonance imaging, and nuclear magnetic resonance imaging. Bio-separation and sensing method, cancer detection/diagnosis, and many more applications. This review comprehensively depicts the methods and challenges in the preparation of magnetic iron oxide nanoparticles as well as their potential application in biomedical fields.

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KEY WORDS: Biomedical technology; Magnetic iron oxide nanoparticles; Drug delivery systems.

Nanoparticles (NPs) are entities typically having a diameter from 1 to 100 nm. Their large surface area to volume ratio empowers them with many advantages for their biomedical applications like lower sedimentation rate, better tissular diffusion, improved bioavailability, high mechanical, thermal stability, etc. In addition, their surface modification can generate materials having desired biological, chemical, and physical properties that make them suitable for specific biological applications.[1]

Magnetic iron oxide nanoparticles (MIONPs) are gaining popularity in various biomedical fields due to their effective size control phenomena, surface characterization along with inherent superparamagnetism property. Their application spectrum includes magnetic resonance imaging (MRI), magnetic particle imaging, biosensing, targeted drug delivery as well as controlled release, in vivo imaging, antimicrobial activities, and many more.[1, 2] Various physical and chemical methods have been developed for the synthesis of MIONPs such as coprecipitation, solvothermal reduction, thermal decomposition, electrochemical synthesis, etc. These methods however suffer from different operational and environmental drawbacks; therefore researchers are now switching to the green routes of their synthesis. MIONPs possess many unique features (Figure 1) like size and shape-controlled properties, surface structure, increased stability, high magnetic response, and most importantly the potentiality to target a specific site for drug delivery.[2] Currently, they have high demand in bio-clinical and diagnostic fields, magnetic bioseparation, evaluation of biological materials like proteins, nucleic acids, enzymes, cells, etc. MIONPs prepared using safe and non-immunogenic materials can effortlessly pass through

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Facile fabrication of Nishamalaki churna mediated silver nanoparticles with antibacterial application

Bhavna Ghosh [a,b], Anindya Bose [a,*], Ankita Parmanik [a], Sanjay Ch [c], Milan Paul [c], Swati Biswas [c], Goutam Rath [a], Debapriya Bhattacharya [d]

[a] School of Pharmaceutical Sciences, Siksha O Anusandhan (Deemed to Be University), Bhubaneswar, Odisha, 751003, India
[b] Sri Jayadev College of Pharmaceutical Sciences, Naharkanta, Via: Balianta, Bhubaneswar, Odisha, 752101, India
[c] Department of Pharmacy, Birla Institute of Technology & Science-Pilani, Hyderabad Campus, Jawahar Nagar, Kapra Mandal, Medchal District, Telangana, 500 078, India
[d] Center for Biotechnology, Siksha O Anusandhan (Deemed to Be University), Bhubaneswar, Odisha, 751003, India

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ABSTRACT

Antimicrobial resistance (AMR) is one of the most serious threats to today´s healthcare system. The prime factor behind increasing AMR is the formation of complex bacterial biofilms which acts as the protective shield between the bacterial cell and the antimicrobial drugs. Among various nanoformulations, green synthesized metallic silver nanoparticles are currently gaining research focus in safely breaking bacterial biofilms due to the inherent antimicrobial property of silver. In the current work, the aqueous extract of the ayurvedic formulation Nishamalaki churna is used to exhibit one pot green synthesis of silver nanoparticles. The physicochemical characteristics of Nishamalaki churna extract mediated AgNPs were evaluated using various analytical techniques, like UV–Visible spectrophotometer, FT-IR spectroscopy, SEM, XRD, DLS-Zeta potential analyzer etc. The synthesized spherical AgNPs were well formed within the size range of 30 nm to 80 nm. Furthermore, the synthesized AgNPs showed potent antibacterial effects against two primary AMR-causing bacterial species like *Staphylococcus aureus* and *Pseudomonas aeruginosa* with the successful destruction of their biofilm formation. Additionally, these AgNPs have shown profound antioxidant and anti-inflammatory activities as desirable add-on effects required by a prospective antibacterial agent.

1. Introduction

Antimicrobial resistance (AMR) is regarded as one of the major health threats in modern times. In the year 2019, an estimated 4.95 million deaths were worldwide reported by various illnesses with as many as 1.27 million deaths by AMR alone. This figure was much higher than the number of people who died due to AIDS or malaria in that year [1]. The continuous reduction in the effective antibiotic options against microbes is the major cause behind this AMR. Furthermore, microbial biofilm formation strengthens resistant microbes by obstructing penetration of antimicrobial agents into them. Biofilms are now responsible for up to 60% of all human infections [2]. In comparison to logarithmic-phase planktonic cells, biofilms are extremely resistant to bactericidal antimicrobials. This antibiotic scarcity against resistant bacteria has created an urgency and highly augmented pressure to invent new therapeutics and strategies to

* Corresponding author.
E-mail address: anindyabose_in@yahoo.com (A. Bose).

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Research Article

Formulation, Development and Evaluation of Sildenafil Citrate Oral Jelly

Braja Bihari Panda[1], Bala Krishna Kala[1], Ankita Parmanik[1], Dattatraya Kar[2], Anindya Bose[1]*

[1] *School of Pharmaceutical Sciences, Siksha 'O' Anusandhan, Bhubaneswar, Odisha-751003, India;* [2] *Department of Medical Research, IMS & SUM Hospital, Siksha 'O' Anusandhan, Bhubaneswar, Odisha-751003, India*

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Abstract

Background: The site of drug administration, such as oral or intravenous, frequently categorizes the route of administration. Drug delivery through oral jelly reduces product costs and enhances product stability and appearance. Oral jelly is used as a drug carrier for different diseases like erectile dysfunction, arthritis, hypertension, and sore throats. Medicated jelly is easy to administer at any time and place without water. ***Aim***: To formulate, develop, and evaluate sildenafil citrate oral jelly. ***Methods***: Oral jelly formulations (F1–F5) with different amounts of excipients and sildenafil citrate were made and tested for things like pH, appearance, viscosity, and drug release in a test tube. The data were analyzed by SPSS version 25 software. ***Results***: The pre-formulation FTIR study revealed that there was no significant interaction between the drug and the excipients used. The pH of all of the formulations was within the desirable range (6.3-6.8), indicating their suitability for product stability and patient acceptability. The stability study indicated that during one-month storage at 25° C and at 40° C/ 75% RH, no significant changes in the properties of the product were found. The viscosity of the formulations increased with increasing sodium CMC concentrations. The HPLC-based in-vitro drug release study indicated that the best drug release was achieved in the F5 formulation. ***Conclusion***: It was concluded that F5 is the formulation of choice satisfying the ideal characteristics of an oral jelly formulation with an improvement in the drug bioavailability over the existing marketed oral formulations of Sildenafil.

Keywords: Sildenafil, Jelly, Spreadability, Extrudability, pH, Stability

صياغة وتطوير وتقييم سيلدينافيل سيترات هلام الفم

الخلاصة

الخلفية: يصنف موقع إعطاء الدواء، مثل الفم أو الوريد، بشكل طريق الإعطاء. توصيل الدواء عن طريق الفم يقلل من تكاليف المنتج ويعزز استقرار المنتج ومظهره. يستخدم هلام الفم كحامل للأدوية لأمراض مختلفة مثل ضعف الانتصاب والتهاب المفاصل وارتفاع ضغط الدم والتهاب الحلق. من السهل إعطاء الهلام الطبي في أي وقت ومكان بدون ماء. **الهدف**: صياغة وتطوير وتقييم هلام الفم سترات السيلدينافيل. **الطرق**: تم تصنيع تركيبات الهلام عن طريق الفم (F1-F5) بكميات مختلفة من السواغات وسترات السيلدينافيل واختبارها بحثا عن أشياء مثل الأس الهيدروجيني والمظهر واللزوجة وإطلاق الدواء في أنبوب اختبار. تم تحليل البيانات بواسطة برنامج SPSS الإصدار 25. **النتائج**: كشفت دراسة FTIR قبل الصياغة أنه لا يوجد تفاعل كبير بين الدواء والسواغات المستخدمة. كان الرقم الهيدروجيني لجميع التركيبات ضمن النطاق المرغوب فيه (6.3-6.8) ، مما يشير إلى ملاءمتها لاستقرار المنتج وقبول المريض. أشارت دراسة الثبات إلى أنه خلال التخزين لمدة شهر واحد عند 25 درجة مئوية وعند 40 درجة مئوية/ 75٪ رطوبة نسبية، لم يتم العثور على تغييرات كبيرة في خصائص المنتج. زادت لزوجة التركيبات مع زيادة تركيزات CMC الصوديوم. أشارت دراسة إطلاق الدواء في المختبر المستندة إلى HPLC إلى أنه تم تحقيق أفضل إطلاق للدواء في تركيبة F5 . **الأستنتاج**: استنتج أن F5 هي الصيغة المفضلة التي تلبي الخصائص المثالية لصياغة هلام الفم مع تحسين التوافر البيولوجي للدواء على التركيبات الفموية الحالية المسوقة من السيلدينافيل.

* ***Corresponding author***: Anindya Bose, School of Pharmaceutical Sciences, Siksha 'O' Anusandhan, Bhubaneswar, Odisha-751003, India; Email: anindyabose@soa.ac.in

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(71)**Name of Applicant :**
1)Siksha 'O' Anusandhan (Deemed to be University)
Address of Applicant :Khandagiri Square, Bhubaneswar - 751030, Odisha, India Bhubaneswar ---------- ----------
Name of Applicant : NA
Address of Applicant : NA
(72)**Name of Inventor :**
1)SAHOO, Rudra Narayan
Address of Applicant :Assistant Professor, School of Pharmaceutical Sciences, Siksha 'O' Anusandhan (Deemed to be University), Odisha - 751003, India Bhubaneswar ---------- ----------
2)NANDA, Ashirbad
Address of Applicant :Associate Professor, School of Pharmacy and Life Sciences, Centurion University of Technology and Management, Bhubaneswar, Odisha - 752050, India Bhubaneswar ---------- ----------
3)PATTNAYAK, Priyabrata
Address of Applicant :Assistant Professor, School of Pharmaceutical Sciences, Siksha 'O' Anusandhan (Deemed to be University), Odisha - 751003, India Bhubaneswar ---------- ----------
4)SATAPATHY, Bhabani Sankar
Address of Applicant :Assistant Professor, School of Pharmaceutical Sciences, Siksha 'O' Anusandhan (Deemed to be University), Odisha - 751003, India Bhubaneswar ---------- ----------
5)ROUT, Sudhanshu Sekhar
Address of Applicant :Associate Professor, School of Pharmaceutical Sciences, Siksha 'O' Anusandhan (Deemed to be University), Odisha - 751003, India Bhubaneswar ---------- ----------
6)PARMANIK, Ankita
Address of Applicant :JRF, DST INSPIRE Fellow (IF-220020), School of Pharmaceutical Sciences, Siksha 'O' Anusandhan (Deemed to be University), Odisha - 751003, India Bhubaneswar ---------- ----------
7)BISWAL, Snehanjana
Address of Applicant :School of Pharmacy and Life Sciences, Centurion University of Technology and Management, Bhubaneswar, Odisha - 752050, India Bhubaneswar ---------- ----------
8)ROUT, Sagar
Address of Applicant :School of Pharmacy and Life Sciences, Centurion University of Technology and Management, Bhubaneswar, Odisha - 752050, India Bhubaneswar ---------- ----------
9)SWAIN, Santosh Kumar
Address of Applicant :Professor, Department of Otorhinolaryngology, IMS & SUM Hospital, Siksha 'O' Anusandhan (Deemed to be University), Odisha - 751003, India Bhubaneswar ---------- ----------
10)PUROHIT, Gopal Krishna
Address of Applicant :CEO & Co-Founder Heredity Biosciences LLP, Plot No: 273/3575, Mayfair Lagoon Road, Jayadev Vihar, Bhubaneswar - 751013, Odisha, India Bhubaneswar ---------- ----------

(57) Abstract :
The present invention generally relates to the field of pharmacology and medical biochemistry. Particularly, the present disclosure relates to a matrix film formulation comprising acetazolamide, silicon dioxide, and triethalonamine; and a process of preparing the same. The present disclosure also relates to a method for retino-protection and intraocular pressure management in a subject having glaucoma and a method for managing glaucoma in a subject in need thereof, by administering the subject with the formulation of the present disclosure.

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