National Research Foundation

SCiENCE MaTTERS

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The Future of Brain Disorder Treatment

CIGARETTE SMOKING: How it affects our oral *microbiota*

Changing Risk of Multiple SARS-CoV-2 Reinfections

OLD Wisdom, NEW Alternatives for Beauty and Skincare

A NEW WAY to heal wounds faster

Solidarity, Equality, Sustainability

A connected world, built on a people-centred and inclusive future

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Addressing today’s needs and protecting our shared future

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This issue of Science Matters highlights the transformative power of research in various fields. It covers revolutionary approaches to cancer drug delivery and wound healing, as well as innovative solutions for treating menopause symptoms and brain disorders. This issue also explores how nanotechnology improves the precision of drug delivery; how extracellular vesicles are leading to new treatments for neurological diseases; and how traditional knowledge is being integrated with modern science to advance skincare.

Scientific innovation continues to shape our world and offers groundbreaking solutions to some of the most pressing health challenges of our time. The NRF would like to thank the researchers who generously shared their research for this issue of Science Matters, allowing us to showcase how South African scientists are making a difference every day.

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TRADITIONAL PLANTS:

Old wisdom becomes new alternatives for beauty and skin care

The health of our skin significantly influences our appearance, prompting many people to use products such as creams and lotions to enhance their skin's look and health.

In the Eastern Cape Province of South Africa, many plants have been used traditionally for these purposes. These plants are thought to help by treating skin problems, protecting against sun damage, and reducing uneven skin tones and spots.

A research study funded by the NRF investigated these traditional plants to determine how effective they really are. The study aimed to connect old wisdom with modern science to potentially lead to the creation of new, natural skincare products. The main goal was to confirm scientifically and measure the skin benefits of these plants by testing their antimicrobial, antioxidant, photo-protective, and anti-tyrosinase properties—all of which are important factors for maintaining healthy skin and creating effective beauty products.

The researchers used detailed methods to test selected medicinal plants. They started with ethnobotanical surveys to identify traditional plants used for skincare and then extracted various compounds from different parts of these plants using different chemicals. These extracts were tested for their ability to:

- Fight common skin germs (antimicrobial activity),
- Protect against oxidation (antioxidant capacity),
- Block or absorb harmful sun rays (SPF),
- Reduce skin pigment production (anti-tyrosinase activity).

The study findings show that plants such as *Arctotis arctotoides* and *Cassipourea flanaganii* were very effective against skin germs such as *Staphylococcus aureus* and *Escherichia coli*, suggesting they could be used in sanitisers and acne treatments. *Cassipourea flanaganii* and *Symphytum officinale* displayed strong antioxidant effects, which could help protect the skin from premature aging due to environmental stress. Extracts from *Plantago lanceolata* and *Cassipourea flanaganii* showed moderate SPF ratings, an indication that they could be acceptable ingredients for use in sunscreen products. Extracts from *Rorippa nasturtium-aquaticum* and *Clausena anisata* inhibited tyrosinase, a key enzyme in skin darkening, which could help in products designed to lighten skin or even out skin tone.

> Extracts from *Rorippa nasturtium-aquaticum* and *Clausena anisata* inhibited tyrosinase, a key enzyme in skin darkening, which could help in products designed to lighten skin or even out skin tone.

This research provides scientific evidence supporting the traditional use of these plants in skincare, showing promising results for their inclusion in future cosmetic products. SM

Full research study https://doi.org/10.1016/j.sajb.2018.05.003

CIGARETTE SMOKING:
How it affects our oral microbiota

The human mouth hosts a diverse ecosystem of bacteria that maintains oral health. However, certain lifestyle factors, such as cigarette smoking, can disrupt this balance and increase susceptibility to oral diseases.

Cigarette smoking is a major public health concern as it contributes to non-communicable diseases such as cardiovascular disease and periodontitis. Tobacco smoke contains harmful toxins that directly interact with the oral microbiota which can lead to bacterial imbalances, increased inflammation, and higher susceptibility to periodontal disease. Previous studies have suggested that smokers have a different bacterial profile compared to non-smokers, characterised by an increase in harmful pathogens and a decline in beneficial oral bacteria.

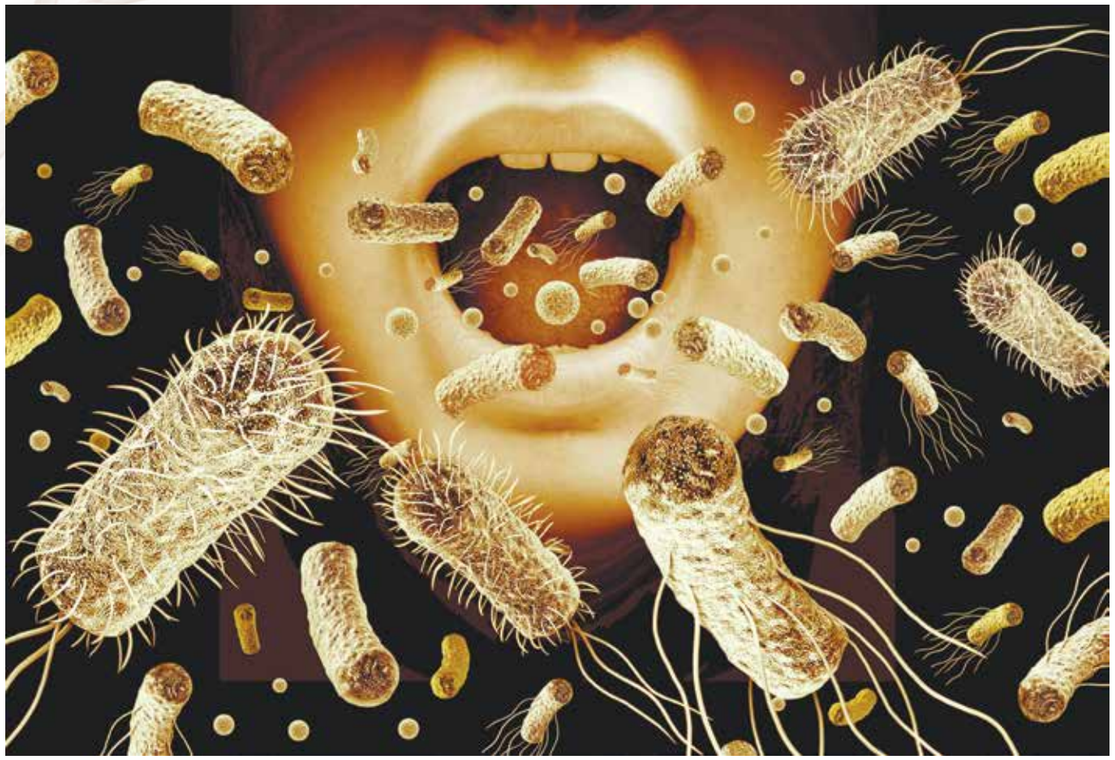
Through the use of subgingival plaque samples and gene sequencing, a research study funded by the NRF investigated how cigarette smoking alters the composition of the oral microbiota. This study sought to determine whether smoking contributes to the proliferation of disease-causing microbes through a comparison between the oral microbiota of smokers and non-smokers. Using 16S rRNA gene sequencing, researchers identified significant differences in bacterial distribution between the two groups.

The researchers recruited 128 participants and categorised them into smokers (57) and non-smokers (66) based on serum cotinine levels (>15 ng/ml). Subgingival plaque samples were collected and analysed to assess bacterial diversity and composition.

The research used advanced metagenomic sequencing to compare bacterial presence at different taxonomic levels, from phylum to species. Statistical analyses were performed to determine the significance of microbiota shifts between smokers and non-smokers.

The study indicated that smokers showed significant changes in their oral microbiota compared to non-smokers. Some key findings included:

- The abundance of Actinobacteria, which plays a vital role in maintaining oral health, was significantly reduced in smokers.
- Smokers exhibited higher levels of *Fusobacterium* and *Campylobacter*, both of which are associated with periodontal disease.
- The presence of beneficial genera, such as *Leptotrichia, Actinomyces, Coryne-bacterium*, and *Lautropia*, was notably lower in smokers, indicating a disruption in microbial balance.
- Smokers had higher concentrations of pathogens, such as *Fusobacterium nucleatum*, *Campylobacter gracilis*, and *Veillonella rogosae*, which are linked to periodontitis and various systemic diseases.



The research findings emphasise that smoking disrupts the oral microbiome which can lead to a microbial environment that fosters periodontal disease progression. Since periodontitis has been linked to cardiovascular disease, diabetes, and other inflammatory conditions, these results highlight a broader systemic impact of smoking on human health.

The research used advanced metagenomic sequencing to compare bacterial presence at different taxonomic levels, from phylum to species. Statistical analyses were performed to determine the significance of microbiota shifts between smokers and non-smokers.

This research reinforces the importance of oral health education and smoking cessation programs to prevent periodontal disease and other related diseases. Further investigations into microbial interventions, probiotics, and personalised oral care strategies could help mitigate the negative effects of smoking on the oral microbiome.

For more details, read the full research study: DOI: 10.1016/j.heliyon.2024.e31559

ASSESSING CHANGES IN RISK for Multiple Reinfections with SARS-CoV-2

In March 2020, the World Health Organization declared the COVID-19 pandemic, which led to a worldwide increase in mathematical modelling to understand how the virus SARS-CoV-2 spreads.

As new variants of SARS-CoV-2 appeared and immunity decreased, it became important to assess the risk of people becoming reinfected by COVID-19.

Understanding the risk of multiple reinfections with SARS-CoV-2 is vital for pandemic preparedness, vaccine strategy optimisation, and public health interventions. While prior research has estimated reinfection risks for first and second infections, little is known about the likelihood of third or subsequent reinfections, particularly in the presence of evolving immune escape variants such as Omicron. The lack of reliable methods to detect and quantify increases in nth infection risks limits our ability to anticipate epidemic trajectories and implement timely health measures.

A research study funded by the NRF expanded on that work through a generalisation of the catalytic model to quantify the risk of third and subsequent infections and applying it to South African reinfection data. The aim of the study was to develop a generalised catalytic model that can detect increases in the risk of multiple reinfections and evaluate its accuracy using simulation-based validation.

The study utilised a national dataset containing daily counts of primary, second, third, and fourth infections of SARS-CoV-2 in South Africa from March 2020 to November 2022. These cases were identified using polymerase chain reaction (PCR) and rapid antigen tests, with reinfections defined as positive tests occurring at least 90 days after a prior infection to distinguish new infections from prolonged viral shedding.

The generalised catalytic model assumed that reinfection risk is proportional to the moving average of detected infections. Using a Bayesian approach, the model fits parameters to observed nth infections while incorporating a hazard coefficient that adjusts for reinfection probability. An additional parameter accounts for increased reinfection risks observed during the Omicron wave.

The study analysis confirmed an increase in reinfection risk during the Omicron wave but did not detect further increases in third infections post-Omicron. This suggests that while Omicron led to enhanced immune escape, subsequent variants have not significantly increased third infection risks.

Simulated validation demonstrated that the model effectively detects increases in third infection risks across different scenarios. When simulated reinfection hazards increased beyond baseline levels, the model successfully identified these changes, confirming its applicability for ongoing surveillance.

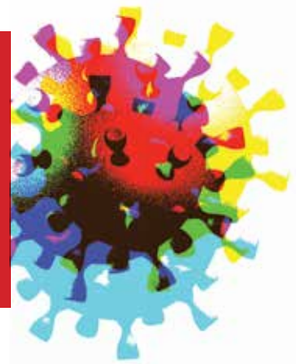
Data from March 2020 to November 2022 revealed a steady rise in second and third infections aligned with new variant emergence. A clear spike in reinfection rates during the Omicron wave. A stabilisation of reinfection hazards followed Omicron, with no substantial increase in third infections thereafter.

The research study successfully generalises the catalytic model to assess the risk of multiple reinfections to provide an important tool for monitoring epidemic progression. The model effectively detected increases in reinfection hazards during the Omicron wave and demonstrated robustness through simulation-based validation.

The findings confirm that Omicron significantly altered reinfection dynamics, emphasising the role of immune escape in epidemic modelling. Despite concerns about evolving variants, the data does not suggest a continued rise in third reinfections post-Omicron.

The study model provides a framework for the assessment of future epidemic risks, allowing for timely public health responses, although further refinement is necessary to extend the model's applicability to fourth and subsequent infections. SM

The full research study can be found at:
https://doi.org/10.1371/journal.pone.0315476



When simulated reinfection hazards increased beyond baseline levels, the model successfully identified these changes, confirming its applicability for ongoing surveillance.

CANCER DRUG DELIVERY: Enhancing Treatment with Nanoparticles and Mathematical Modelling

Nanoparticles (NPs) present a promising advancement in targeted cancer therapy, offering the potential to deliver drugs directly to tumour cells while minimising the harmful side effects of traditional chemotherapy.

Unlike conventional treatments, NP-based drug delivery systems can be engineered to improve drug accumulation in tumours, enhance treatment efficacy, and reduce toxicity in healthy tissues. However, several barriers hinder their clinical success, including drug resistance, challenges in targeting tumour cells with precision, and biological barriers within the tumour microenvironment that restrict drug penetration.

To improve the effectiveness of NP-based treatments, researchers employ mathematical models that predict how drug-loaded nanoparticles interact within the body. These models consider nanoparticle properties such as size and composition, tumour characteristics, and physiological responses to optimise drug delivery strategies. However, current models often rely on oversimplified assumptions that lead to inaccurate predictions of drug transport and treatment efficacy. The complexity of cancer biology requires more refined and adaptive modelling techniques to ensure that these predictions closely align with real-world therapeutic outcomes.

A research study funded by the National Research Foundation (NRF) explored the role of nanoparticles in cancer drug delivery, with a particular focus on how mathematical modelling can be used to enhance treatment precision and optimise NP-based therapies. The study examined the limitations of current computational approaches and emphasised the need for more accurate, data-driven models that can predict drug distribution, accumulation, and therapeutic success in both preclinical and clinical settings.

To achieve this, researchers aimed to integrate artificial intelligence (AI) and machine learning techniques into traditional modelling frameworks, allowing for more precise simulations that account for tumour variability and patient-specific factors.

One of the major challenges in NP-based drug delivery is drug resistance, where tumour cells develop mechanisms to evade or neutralise therapies over time. This reduces the long-term effectiveness of nanoparticle treatments and requires adaptive treatment strategies to overcome resistance. Another critical barrier is targeting specificity, as achieving high precision in the delivery of drugs to tumour cells while sparing healthy tissues remains difficult. Additionally, the tumour microenvironment poses a significant challenge, as its complex structure—including abnormal blood flow, dense tissue networks, and immune system interactions—can limit the penetration and uniform distribution of nanoparticles. These obstacles highlight the need for advanced modelling techniques that consider biological complexity to improve drug delivery predictions.

Mathematical models play a crucial role in predicting and optimising NP interactions with tumours and physiological systems. By analysing nanoparticle behaviour under different conditions, researchers can determine the optimal size, shape, and surface properties of nanoparticles to maximise drug delivery efficiency. Models also help simulate how nanoparticles move through the bloodstream, accumulate in tumours, and release drugs over time, allowing scientists to refine treatment regimens for better outcomes. The integration of computational simulations with AI-based learning models further enhances predictive accuracy, enabling more personalised treatment approaches based on individual patient characteristics.

The study suggests that to translate NP-based cancer therapies into clinical practice, research should focus on refining nanoparticle design for improved targeting, controlled drug release, and reduced toxicity. Additionally, developing more sophisticated mathematical models that incorporate real-world biological interactions will be key to ensure that predictions align with actual patient responses. The integration of AI-driven models with experimental and clinical data can further enhance treatment personalisation, ultimately improving therapeutic success rates.

While current models provide a solid foundation, there is a pressing need for more dynamic and multi-scale approaches that consider the biological, chemical, and physical interactions of nanoparticles at different levels. By bridging the gap between experimental research and clinical application, these advancements could revolutionise cancer treatment strategies and make nanoparticle-based drug delivery a more viable and effective option for patients.

Nanoparticles hold great potential in transforming cancer drug delivery, but to fully realise their benefits, biological and computational challenges must be addressed. Mathematical modelling remains a powerful tool in refining NP-based therapies, making them more precise, adaptable, and clinically viable. With ongoing advancements in nanotechnology, AI, and computational modelling, future therapies may offer more effective, personalised cancer treatment solutions, significantly improving patient outcomes. SM

For further details, read the full research study:
https://doi.org/10.3390/cancers17020198

> The integration of AI-driven models with experimental and clinical data can further enhance treatment personalisation, ultimately improving therapeutic success rates.

EXTRACELLULAR NANOVESICLES:

A new way to treat brain disorders

The treatment of central nervous system (CNS) disorders remains a major global health challenge.

Disorders, including Alzheimer's, Parkinson's, multiple sclerosis and stroke, affect the brain and spinal cord tissues and, depending on where they manifest in the CNS, they impair cognitive and motor functions, disrupt the blood-brain barrier (BBB), and damage neurons.

The BBB is a natural shield that protects the brain, but it also makes it difficult for medicine to enter. It is one of the biggest challenges in treating CNS disorders. Current treatments for brain disorders often fail because they cannot effectively cross the BBB, which limits their success while existing drug delivery methods can be invasive, expensive, or cause unwanted side effects. These challenges highlight the urgent need for innovative approaches to safely deliver therapeutic agents across the BBB.

An NRF-funded research Chair, Prof. Yahya Choonara and his team, reviewed the potential of extracellular vesicles (EVs) as an innovative drug delivery system capable of transporting medicine directly to the brain in a safe and effective manner. EVs are membrane-bound vesicles derived from cells, tissues, or plant materials, that offer natural biocompatibility and therapeutic potential. They can carry medicine, cross the BBB, and deliver treatment where it is needed. These vesicles are safe, can be modified for better results, and may help improve treatments for brain diseases.

The study aims to:

- Determine whether EVs can cross the BBB and reach brain cells.
- Assess the effectiveness of EVs in delivering medicine to treat conditions such as Alzheimer's, seizures, brain cancer, and traumatic brain injuries.
- Compare EVs to existing treatments in terms of efficiency, safety, and side effects.
- Identify challenges in EV-based treatments, such as production difficulties, ethical concerns, and immune system reactions.
- Suggest improvements to make EV treatments more practical and widely available in the future.

The researchers extracted EVs from human cells, cow's milk, and plants to study their shapes and sizes. They then created a model of the blood-brain barrier (BBB) using human brain cells to investigate whether EVs could pass through it. To enhance their targeting ability, they modified the EVs by adding medicine or special molecules designed to target brain cells. Finally, they tested these modified EVs in animal models, specifically in mice with brain diseases, to determine if the treatments led to any improvements.

Research key findings show that:

- The human plasma-derived EVs successfully passed through the BBB and remained in brain cells longer than other treatments.
- Cow's milk-derived EVs easily reached the brain and promoted brain cell growth.
- Brain cell-derived EVs were loaded with medicine and directly targeted brain tumours.
- EVs loaded with resveratrol (a natural antioxidant) reduced brain inflammation.
- EVs carrying GABA (a brain-calming chemical) helped reduce seizures.

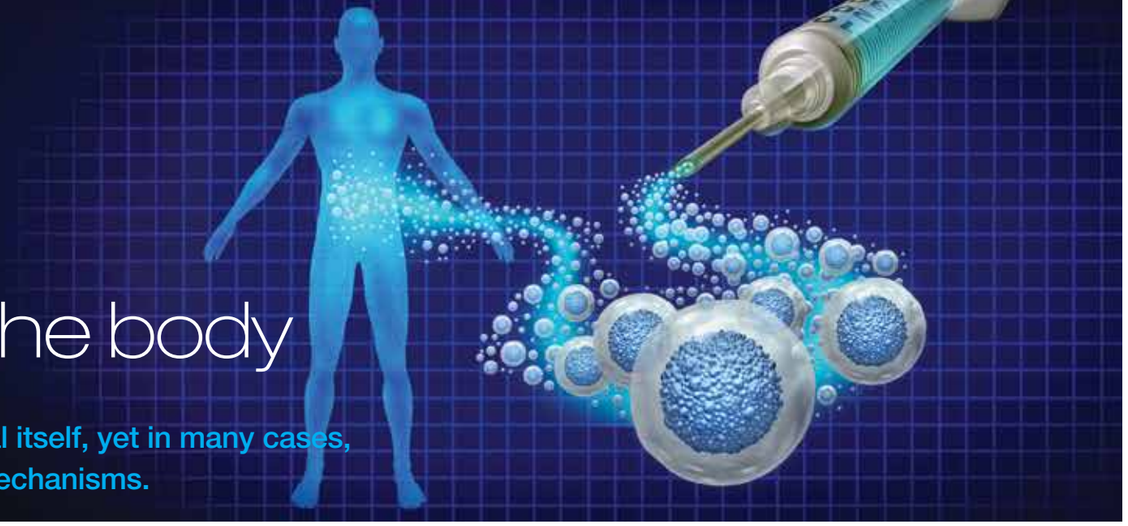
To enhance their targeting ability, they modified the EVs by adding medicine or special molecules designed to target brain cells.

While EVs show great promise, there are several challenges that still need to be faced. The production of large quantities of EVs for medical use is difficult and expensive. Not all EVs work the same way, which makes it hard to achieve consistent results. Using human-derived EVs, such as those from breast milk, raises ethical concerns. It is crucial to ensure that EVs do not trigger unwanted immune responses. SM

For more details, read the full research study: https://doi.org/10.1080/17425247.2024.2440099

STEM CELL SECRETOME:

A new way to heal the body



The human body has an extraordinary ability to heal itself, yet in many cases, injuries and diseases surpass their natural repair mechanisms.

This has led researchers to explore regenerative medicine strategies that can enhance healing processes, particularly for conditions such as heart disease, nerve damage, and chronic wounds.

One of the most promising developments in this field is the stem cell secretome, a complex mixture of bioactive molecules released by stem cells. These molecules, which include proteins, growth factors, cytokines, and extracellular vesicles (EVs), have shown significant potential in tissue regeneration, wound healing, and organ repair.

Over the years, stem cell therapy has been widely studied as a regenerative treatment, relying on the transplantation of stem cells into injured tissues. However, several challenges limit its clinical application, including immune rejection, ethical concerns, tumorigenic risks, and the difficulty of ensuring stem cell survival post-transplantation. Recent scientific advancements suggest that the therapeutic effects of stem cells may be largely mediated by their secretions rather than the cells themselves.

A research study funded by the NRF evaluated how secretome can provide clinically relevant pharmaceutical targets and act as clinical novel therapies. In addition, the research also considered the advancements and achievements made in the field, focussing on the implication of the secretome in health and disease as well as the secretome as a biotherapeutic agent.

The study evaluated the therapeutic potential of secretome-based treatments for wound healing, neuroregeneration, and cardiac repair. It also identified the challenges and limitations that must be addressed for clinical translation.

To assess the therapeutic potential of the secretome, researchers cultured mesenchymal stem cells (MSCs) in the laboratory and collected the bioactive molecules they secreted into the surrounding medium. These secreted factors, consisting of proteins, cytokines, and extracellular EVs, were then analysed using high-throughput proteomic technology to identify the key molecules responsible for tissue regeneration.

The secretome was tested on models of wound healing, spinal cord injuries, and heart damage to evaluate its effectiveness in promoting recovery. The results were compared against traditional stem cell therapies to determine whether the secretome could match or surpass their regenerative effects.

The study yielded remarkable results, demonstrating that the secretome enhances tissue repair and regeneration across multiple medical applications. In wound healing models, secretome treatment accelerated wound closure by 35% compared to untreated wounds. The presence of growth factors within the secretome led to a 45% increase in angiogenesis, improving blood supply and oxygenation to the damaged tissue. Additionally, secretome therapy stimulated collagen synthesis, resulting in stronger, better-organised scar tissue, which is crucial for restoring skin integrity.

In models of spinal cord injury, the secretome exhibited a 50% improvement in movement recovery, suggesting its potential in neuroregeneration. Furthermore, nerve inflammation was reduced by 40%, minimising secondary damage and creating a more favourable environment for healing. A 30% increase in nerve fibre regrowth was also observed, indicating that the secretome supports neural repair mechanisms and functional recovery.

The research also explored the secretome's impact on cardiac tissue repair following heart injury. In heart attack models, secretome treatment improved cardiac function by 28%, significantly enhancing the heart's ability to pump blood. Additionally, blood vessel formation increased by 50%, facilitating better circulation and tissue oxygenation. Notably, harmful inflammatory markers were reduced by 40%, demonstrating the secretome's potential in limiting post-injury inflammation and fibrosis.

> Standardisation is crucial to ensure consistent therapeutic outcomes across different batches.

Another critical area of investigation was the secretome's ability to reduce organ scarring. In liver and lung injury models, scarring was reduced by 60%, a significant improvement compared to conventional treatments. This reduction in fibrosis is essential for restoring normal organ function and preventing long-term damage. The antioxidant properties of the secretome also played a key role, protecting cells from oxidative stress and promoting healthier tissue regeneration.

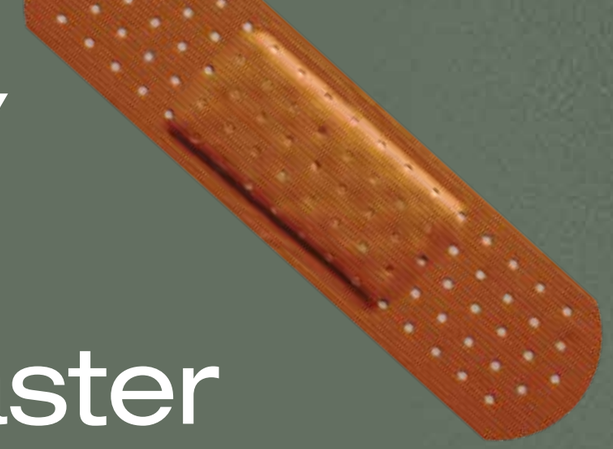
However, despite its promising therapeutic potential, several challenges must be addressed before secretome-based therapies can be widely adopted in clinical practice. One major challenge is the variation in secretome composition, which depends on the type of stem cells used, their growth conditions, and external stimuli. Standardisation is crucial to ensure consistent therapeutic outcomes across different batches.

Another challenge is the stability and delivery of secretome components. The molecules within the secretome degrade quickly, which can reduce their effectiveness. To address this issue, researchers are developing innovative delivery methods, such as hydrogels, nanoparticles, and encapsulated formulations, to enhance stability and prolong the therapeutic effects.

The study concluded that the stem cell secretome represents a transformative advancement in regenerative medicine, offering a cell-free alternative to traditional stem cell therapy. By leveraging the bioactive molecules released by stem cells, scientists can develop effective, scalable, and safer treatments for tissue repair and organ regeneration. With ongoing technological innovations, clinical trials, and regulatory progress, the future of cell-free healing solutions appears exceptionally promising. SM

For further details, read the full research study: https://onlinelibrary.wiley.com/doi/10.1111/wrr.13251

A NEW WAY to Heal Wounds Faster



The skin is the body's largest organ and acts as a protective barrier. However, injuries such as cuts, burns, and surgical wounds can damage the skin, leading to pain, infections, and slow healing.

While the body can repair itself, some wounds take too long to heal, which can cause complications such as infections or scarring. Scientists are constantly looking for better ways to speed up wound healing and improve recovery.

A research study funded by the NRF developed a special collagen mimetic peptide (CMP) hydrogel designed to help the skin heal faster. This new material, which contains synthetic peptides that mimic the natural structure of collagen, was tested in laboratory and in animal studies to see if it could improve wound healing. The results suggest that this hydrogel may be a promising new treatment for people with slow-healing wounds.

The goal of this research was to create a wound dressing that speeds up healing by mimicking natural collagen. Collagen is an important protein that helps the skin repair itself after an injury. The scientists designed a special CMP and combined it with hyaluronic acid, a substance that helps wounds stay moist and supports cell growth. The researchers then tested whether this hydrogel could improve wound healing when applied to human skin cells and animal wounds.

To meet their research goals, the researchers created and improved two peptides, NL008 and NL010, using adamantane to enhance their effectiveness. They mixed the peptides with hyaluronic acid to form a hydrogel suitable for treating wounds. They tested the hydrogel's safety by exposing human skin cells to it. They also performed scratch tests to see how fast the hydrogel helped cells close fake wounds. The researchers applied the hydrogel to wounds on rats and checked the healing progress after 3, 7, and 14 days. They used pig skin to see if the hydrogel could penetrate and remain in the skin.

The scientists designed a special CMP and combined it with hyaluronic acid, a substance that helps wounds stay moist and supports cell growth.

The study found that the NL010 peptide was the most effective for wound healing. The main results were:

1. Faster Wound Closure

- In human skin cell scratch tests, the NL010 hydrogel achieved 99.9% wound closure within 24 hours, while NL009 achieved 93.7%.
- The control (untreated) wounds took much longer to close, showing that the hydrogel speeds up healing significantly.

2. Peptide Release and Absorption

- The hydrogel released 83% of its peptides over time, ensuring a steady supply of healing molecules.
- In pig skin tests, the hydrogel penetrated the epidermis and stayed in the upper layers of the skin, making it effective for wound treatment.

3. Improved Healing in Animals

- In rat wound healing experiments, the NL010 hydrogel led to faster healing compared to untreated wounds.
- Treated wounds showed better epithelialization (skin cell regrowth) and increased collagen production, which are both important for proper healing.
- By day 14, wounds treated with the NL010 hydrogel were almost completely healed, while untreated wounds were still in the early stages of recovery.

4. Hydrogel Strength and Texture

- The hydrogel had a porous structure (<30 µm), which helps in absorbing wound fluids and allowing skin cells to grow.
- It was also biocompatible, meaning it did not harm skin cells.
- The hydrogel had a stronger texture compared to regular hyaluronic acid, making it a good candidate for wound dressing applications.

This study shows that a CMP hydrogel can significantly improve wound healing by speeding up skin cell migration, increasing collagen production, and enhancing wound closure. The NL010 hydrogel was particularly effective, demonstrating 99.9% wound closure in lab tests and fast healing in animal studies. If further developed, this hydrogel could become a valuable new treatment for wounds, especially for people who struggle with slow-healing injuries. SM

Full study : https://doi.org/10.1021/acsabm.4c01895 -

THE NEW HYDROGEL-BASED Vitreous Substitute for Eye Treatment

The vitreous is a clear, gel-like substance that fills the back of the eye, providing structural support and helping to maintain vision. However, certain retinal diseases, such as retinal detachment and proliferative vitreoretinopathy (PVR), require the vitreous to be removed through vitrectomy surgery.

Current vitreous substitutes, such as silicone oil, have limitations, including causing cataracts and toxic effects on the eye. To address these issues, researchers have developed an innovative hydrogel-based vitreous substitute that can also deliver drugs to treat post-surgery inflammation and other eye diseases.

The goal of this NRF-funded research was to develop a thermoresponsive hydrogel-based vitreous substitute that can mimic the natural vitreous while also acting as a drug delivery system. The hydrogel is designed to be biodegradable, injectable, and capable of sustained drug release, reducing the need for repeated eye injections.

Researchers created a hydrogel using hyaluronic acid (HA) and poloxamer polymers, which are biocompatible materials commonly used in medical applications. To enhance its therapeutic properties, they loaded the hydrogel with PLGA nanoparticles containing triamcinolone acetonide (TA), an anti-inflammatory drug used to treat post-vitrectomy inflammation and retinal diseases.

The hydrogel was tested for:

- Gelation time - how quickly it forms a gel at body temperature
- Drug release behaviour - how long it releases the drug over time
- Biocompatibility - its safety for human cells
- Swelling and degradation - how stable it is in the eye environment
- Injectability - how easily it can be administered through a small needle
- *In vivo* performance - tested in rabbit models to see if it works in a real eye

The hydrogel is designed to be biodegradable, injectable, and capable of sustained drug release.

The hydrogel demonstrated fast gelation within nine to ten minutes at body temperature, making it suitable for clinical use. It remained stable in the eye for over 28 days and maintained its optical transparency (90%), closely mimicking the natural vitreous. The hydrogel effectively released 50% of the drug within the first seven days, followed by a slow, controlled release over nine weeks, reducing the need for frequent eye injections. It showed high biocompatibility, with no significant toxicity in lab-grown human retinal cells and minimal inflammation in rabbit eye tests. The hydrogel's mechanical properties were also similar to the natural vitreous, ensuring proper retinal support and maintaining vision. SM

Full research study : https://doi.org/10.1007/s13346-024-01566-1

Lessons drawn from mother nature's recipe book

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Dr Monique Engelbrecht-Roberts & Dr Randall Fisher, Radiobiology Scientists, NRF-iThemba LABS

South Africa is one of the most biodiverse countries in the world, with more than 87 400 documented plant and animal species. Mother Nature provides a context filled with intrigue, surprise, revelation, insight, opportunity and challenges that guide our research and innovation to create a better tomorrow. But what are some of the lessons that we can learn from careful observation and interpretation? Could it be that, apart from her beauty, she also offers solutions to some of the world's most challenging healthcare problems, such as cancer and wound healing?

One would expect that large mammals such as whales and elephants, with their large bodies made of trillions of cells, would have a much higher risk of developing cancer when compared to humans. In reality, we find that these mammals have evolutionary mechanisms that render them cancer-resistant. This phenomenon, known as Peto's Paradox, suggests that Nature has fine-tuned these large mammals to overcome cancer using various hidden strategies. In elephants, cancer-resistance is suspected to be related to the 14 to 20-fold higher copy number of the "guardian-of-the-genome" or tumour-suppressor gene (TP53), found in the elephant's DNA. This gene encodes a protein that manages the decision for the cell to either "self-repair" or "self-destruct," depending on the complexity of the DNA damage in the cell. We suspect that the abundance of TP53 may cause elephant cells to rather self-destruct, than to become cancerous. The solution to cancer is not as simple as increasing the TP53 copies in humans, as labs that have attempted this in other animals, have seen accelerated aging. For now, we only know part of the story.

From plants, we learn some interesting secrets about wound healing: In the Western Cape, *Aloe ferox, Aloe vera*, and *Carpobrotus edulis* (Sour fig) have long been used by traditional healers to treat skin wounds and ailments. These ailments range from hyper-or-hypo pigmentation of scars, damage to tissue after medical procedures, or scars resulting from skin infections. Laboratory testing of extracts from these plants indicate high levels of phenolic compounds with strong antioxidant activity. These extracts show anecdotal evidence of improving skin recovery after damage, but their ability to protect cells against damaging-radiation is yet to be determined.

So, how do we transform these insights into an impactful research agenda? At the Radiation Biophysics division of NRF-iThemba LABS in Cape Town, we compare the cellular responses of elephant and human blood- and skin-cells, after radiation-induced DNA damage, to understand Nature's mechanisms of cancer resistance. This project, in collaboration with the University of the Western Cape (UWC), the German Science Institute Helmholtzzentrum für Schwerionenforschung, private game reserves at Botlierskop and Gondwana in the Garden Route, and the African Wildlife Conservation Foundation, aims to discover what makes elephants cancer resistant. Understanding this mechanism might open doors for gene-therapy-based cancer treatments to support conventional cancer treatment. In partnership with the Skin Research Lab at UWC, we investigate the radioprotective and radiomitigator effects of plant extracts used by Western Cape indigenous communities to treat skin ailments and wounds. These natural extracts may have the potential to protect skin cells against radiation-induced DNA damage by "mopping up" the free-radicals or reactive-oxygen molecules formed after ionising radiation exposure. Extracts that display radioprotective capabilities may be used in supportive or topical medical applications for patients receiving radiotherapeutic cancer treatments.

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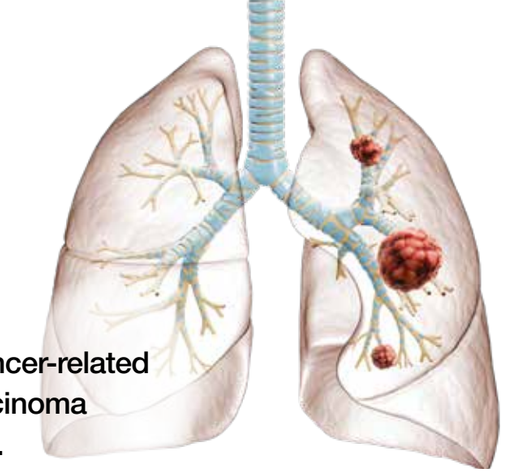
Laboratory for Accelerator Based Sciences

A New Approach to LUNG CANCER TREATMENT



Lung cancer is one of the leading causes of cancer-related deaths worldwide, with non-small-cell lung carcinoma (NSCLC) accounting for about 85% of all cases.

One of the most commonly used chemotherapy drugs for NSCLC is paclitaxel (PTX), but its effectiveness is limited by poor water solubility, rapid degradation, and harmful side effects on healthy cells. Scientists have been searching for better drug delivery systems to improve PTX's ability to target cancer cells while reducing side effects.

A research study funded by the NRF on Prototyping 21st Century Nanomedicines and Advanced Drug Delivery Technologies, has developed a new nanocarrier system using mesoporous polydopamine (mPDA) nano-bowls to deliver PTX directly to cancer cells. These bowl-shaped nanoparticles are designed to improve drug loading, enhance stability, and release PTX in response to the acidic environment of tumours. Their findings suggest that this innovative nano-drug system could enhance lung cancer treatment.

The study aimed to create a more effective drug delivery system for PTX using mPDA nano-bowls. The researchers designed these nanoparticles to efficiently entrap PTX, release the drug in a controlled manner, and suppress lung cancer cell growth. The primary objectives were to test the loading capacity, drug release behaviour, and effectiveness of the nanocarrier against NSCLC cells.

> The nanoparticles significantly suppressed A549 lung cancer cell proliferation.

The team synthesised mesoporous polydopamine nano-bowls through a process called emulsion-induced interfacial anisotropic assembly. These nano-bowls were loaded with PTX, forming mPDA-PTX-nb, and were tested using different scientific experiments and procedures.

The research findings show that, the nano-bowls demonstrated excellent drug-loading efficiency, successfully entrapping 95.7% of PTX, with 85.1% of the drug being released under acidic tumour-like conditions over 48 hours. This controlled release pattern helped target cancer cells more effectively while reducing exposure to healthy cells, where only 36.5% of PTX was released at normal pH levels. The nanoparticles significantly suppressed A549 lung cancer cell proliferation, reducing cancer cell viability to 14.0% after 48 hours and 9.3% after 72 hours, which was a stronger effect than standard PTX treatments. Moreover, the mPDA nano-bowls remained stable in solution for at least seven days and showed no toxicity to healthy human cells, confirming their potential as a safe and effective drug delivery system.

In conclusion, this study introduces a promising new nanocarrier for lung cancer treatment by targeting tumors directly and minimizing exposure to healthy cells. SM

Full research study : https://doi.org/10.3390/pharmaceutics16121536 -

A New Intrauterine Device for Treating **MENOPAUSE SYMPTOMS**

Menopause is a natural stage in a woman's life that brings several changes, including a decrease in oestrogen levels. This can lead to genitourinary syndrome of menopause (GSM), which causes symptoms such as vaginal dryness, pain during intercourse, and urinary problems.

Many women use oestrogen therapy to relieve menopause symptoms, but the current treatments—such as creams, pills, and vaginal rings—have drawbacks such as frequent dosing, messiness, and discomfort.

A University of the Witwatersrand (Wits) research team, funded by the NRF developed a new intrauterine device (IUD) that releases hormones in a controlled way over a long period. This multi-component drug delivery system (MCDDS) could provide a more effective and convenient way to treat GSM. The study aimed to create an implantable intrauterine device that delivers two hormones—oestradiol hemihydrate (E2) and norethindrone acetate (NETA)—directly to the uterus.

The researchers designed a hollow cylindrical drug delivery system (EPHCD) that slowly releases oestradiol. They combined it with a polymeric matrix (NLPM) that releases norethindrone acetate to create the MCDDS intrauterine device. The study tested the chemical composition to ensure the hormones remained stable and examined the surface and structural properties to check the device's durability and texture.

The study found that the EPHCD component released 23.78% of estradiol over four weeks, with a slow and steady release pattern. The MCDDS released 23.67% oestradiol and 38.05% norethindrone acetate over the same period. Mathematical modelling predicted that the IUD could continue releasing oestradiol for up to 25 weeks and norethindrone acetate for 15 weeks. The MCDDS also showed excellent biocompatibility, as it did not harm human fibroblast cells, maintaining over 70% cell viability in laboratory tests. The materials used in the device were safe and non-toxic, making it a potential long-term treatment option.

This study presents a groundbreaking approach to the treatment of menopause symptoms. It has the potential to be a more effective, safer, and patient-friendly alternative to current hormone therapies. SM

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Full research study: https://doi.org/10.3390/polym17050665

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