

SURVIVAL OF A SILENT MONSTER IS IN DANGER

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PLEASE Help....!!!
My future survival will be in danger....!!!

Today, I will tell you my sad story. 😞😞😞

I am periodontitis, and I am proud to tell you that I am the 6th most prevalent disease, and approximately 11.2% of people around the world are suffering because of me. In India itself, poor oral hygiene has helped me a lot, and around 90% of people are in pain because of me. I am thrilled to tell you that despite being native to the mouth, I am associated with systemic diseases like coronary heart disease, respiratory tract infections, diabetes, pre-term birth, and oral cancers as well.

You are surprised! Unclean mouths can be this deadly! That's how I cause the burgeoning health issues that often go unnoticed. Unclean mouths and poor oral habits of the ignorant population are my well-wishers. They help me thrive and sustain! Blessings galore!!

You must be curious to know how it is possible?

Interested!!!

Well!

Let me spill the beans!

You fall in love with that toothy smile! I caught you!!

Right!

Ha Ha...

Right there around your pink gumline, I keep following your ravishing smile. Creepily! Steadily! Bit by bit! You ignore my presence!

Careless you!

I stay put, and my loyal opportunistic soldiers without being caught reach the other body organs. When the host army (inflammatory cells) try to act smart, I win over them by triggering the production of chemicals which ultimately bring the castle down.

So, the strategy is to enter their domain, debilitate them be persistent, and survive the game!!!

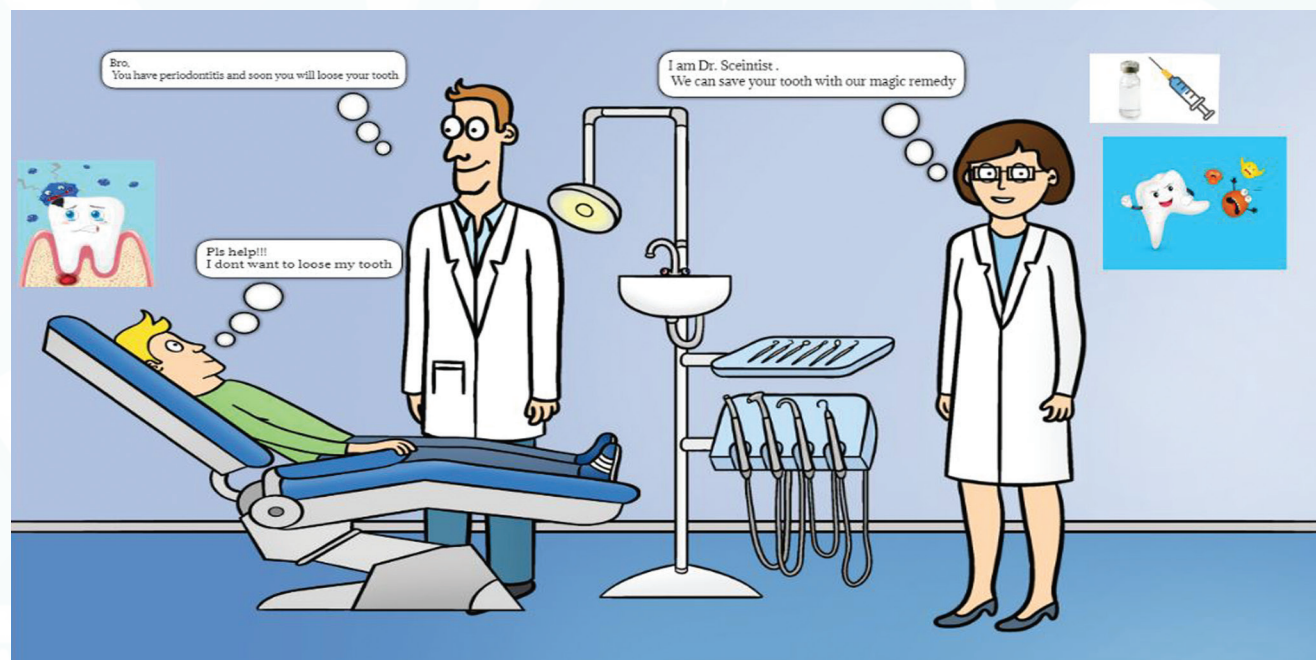
It gives me immense pleasure to apprise you that my friend COVID-19 has also helped me a lot. When the whole world was in lockdown, people just thought dental visits could be postponed, and mouth hygiene wasn't that important. That's what I needed to become a monstrous problem with more power at hand. I was pleasantly surprised that researchers had unravelled my ties with COVID-19, and those beautiful memories would remain my legacy for all days to come.

Before going ahead, I must tell you about my nexus. Poor oral hygiene helps me to take birth in a mouth. First, my loyal brigade of *Porphyromonas gingivalis*, *Prevotella intermedia* and others become active and dominant on the tooth surface and gum linings. They create a protective blanket for their survival and increase their population under the blanket or so-called biofilm. The blanket acts as a shield against antibiotics.

See...How smart my soldiers are!

Next to this, activated host cells trigger the COX-II enzyme, which generates cytokines leading to swelling of gums and pain. As time passes, the MMP enzyme from gums degrades tooth supporting structure-collagen. This results in the development of pockets between teeth and gums. Do you know this pocket can be 2-8 mm deep? In an aggressive state, the tooth bone degrades leading to tooth fall. And in this way, my vicious circle continues.

If I am very sure all this scenario is happening in a neglected mouth. Not all, but few brush me off, making the



surface squeaky clean and making my life a bit difficult! A shiver goes deep down my mantle as the hosts visit a dental clinic, but, much to my glee, blatant use of high-dose oral antibiotics prescribed by the dentists results in antimicrobial resistance and unnecessary exposure to the non-site body parts. Not only this, dentists prescribe multi-drug therapeutics like painkillers and bone regenerating agents along with antibiotics, which altogether lead to high-cost therapy and patient non-compliance. All these conventional and surgical procedures are expensive and non-affordable.

Therefore, no such strategy is available which could completely give relief to patients from my terror.

But recently, I got the news that the research group of Dr Scientist has been secretly working on periodontal drug delivery systems with the aim of a surgical strike against me. I read that, in the past, they have developed multi-component gingiva disc for initial stage periodontitis. But this time, this crazy group have developed a multi-component *in-situ* gel to fight against my trustworthy soldiers and has decided to destroy my life cycle completely. They collected all the information about me from every possible source like Google Scholar, PubMed, and research gate, etc. and selected targeted agents against me. Paul Ehrlich's "magic bullet" concept seems to be their biggest motivation. I am now a bit disturbed. What they did was not leave any stone unturned to find what would pointedly work against my army. After time-consuming careful investigation, they selected biofilm-forming proteins of *Porphyromonas gingivalis*, such as InlJ and RGPB, and with the help of a computer based *in-silico* study, they compared the binding capacity of minocycline, the major killer antibiotic with them. They also checked the affinity of celecoxib drug with COX-II enzyme, Doxycycline with MMP enzyme and Hydroxyapatite with bone receptor. They found that all the selected agents have a good binding capacity with the targeted receptors. This study served as a proof of concept for them, and they treated it as hypothesis validation. Moreover, the group has published this report in a well-known peer-reviewed journal of Bentham science publishing house.

The next challenge for the group was to incorporate all the agents in a singular system for sequential release. So, they created a compartmental strategy or else can be called as a smaller box inside a larger box (disc in disc approach).

With the aim to develop a perfect product they assessed all the risk variables that could affect the properties of the final product. For this, they relied on the prevalent IT tools like Design Expert and Lean QbD.

This was indeed a great novelty, never heard before. First, they developed, nanoparticles of hydroxyapatite and doxycycline. Next to this, they fabricated celecoxib and nanoparticles containing microcapsules. Lastly, they loaded these microcapsules and minocycline in an *in-situ* gel system. The team comprised dedicated research scholars who were constantly in touch with the dental practitioners who guided them to create a product which would be a solution

at refrigerator temperature and convert into a stable gel in periodontal cavity. With this aim, they developed and characterised the *in-situ* gel for viscosity, syringe ability, flow behaviour and gel strength. Their work progress was stupendous, and all stability studies went well.

The next crucial part of their research was bioactivity studies, which were categorised into three parts — cell line study, biofilm study and animal study.

For the cell line study, they had taken the institutional ethical committee approval and with due patient consent, they collected the 3rd impacted healthy pre-molar teeth from patients attending the dental OPD of a reputed hospital. Ligament cells were extracted from the molars and cultured in a well-equipped lab of Molecular Medicine. They observed significant cell growth with *in-situ* gel. For biofilm also, they collected the plaque samples from the periodontal pocket of 30 patients attending the Dental OPD. They cultured the samples and, unfortunately, caught my two favourite soldiers *P. gingivalis* and Prevotella species. They developed the biofilm in a microbiology lab of the said hospital and they found that their *in-situ* gel was successful in inhibiting and eradicating the biofilms of both organisms. Dr Scientist group was very happy to see this, but they wanted to confirm it with animal studies.

So, for the animal studies, they got clearance from the Institutional Animal Ethics Committee and developed experimental periodontitis in New Zealand White rabbits by tying the silk sutures around the teeth of rabbit. After disease induction and treatment with *in-situ* gel, they observed considerable improvements in tooth mobility, bleeding on probing, gingival index and alveolar bone loss. However, at this stage, to take proper care of animals, they followed the ARRIVE guidelines.

I am scared and enthralled to see the complexity of the work done by Dr Scientist group. They imperilled the lives of my soldiers. They have taken a bold step to work on an ignorant disease and have turned all the stones left for the disease treatment. Their first aim was to abolish my existence, and the second was to make the treatment affordable for patients. They were successful in reducing the dose as well. Surely, it will be a generous gift for their society.

I am afraid that if the group continues to work in this manner, then the day is not far when I shall lose my prestigious 6th position in the diseases chart and might fall prey to this "magic bullet" created to annihilate one of the most prevalent diseases on the earth surface. I am afraid my days amidst this beautiful environ of pink streets of gumlines are numbered, and very soon, I will be a bugger off from the earth and meet the same fate as met by my friend Polio.

I am doomed!!

Awwwww.... 😞

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