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Research Article,

Development of a Drug Eluting Self Expandable Bioresorbable Scaffold System to Treat Rhino-Sinusitis

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Abstract:

In the present research work, an idea of implanting self-expandable bioresorbable sinus scaffold system and its development strategies have been portrayed in order to treat sinusitis caused into the tissue linings of the sinuses. The device utilized here is made up of bioresorbable material which is a kind of co-polymer which is an inactive ingredient. This device is additionally coated with an anti-inflammatory drug with another inactive ingredient, which helps to elute or release the drug in a controlled manner and degrade the device over a period prior to dissolving. By performing *in vitro* test, it has been indemnified that, this drug coated device is relevant and promising to treat sinus inflammations.

Keywords: Sinus, sinusitis, self-expandable, bioresorbable materials, scaffold, drug.

Introduction:

Sinuses are the hollow cavities inside the bones between the eyes, behind the cheekbones, as well as in the forehead. They do the function of forming mucus which keeps the nasal passage in a moist condition. Sinusitis is a condition in which the tissue linings of the sinuses get inflamed or swollen. There are total four pairs of sinuses as shown in the fig.01 namely 1) Frontal sinuses- found into the frontal bone around lower part of the forehead followed by eye sockets and eyebrows 2) Maxillary sinuses- found into the maxillary bones around the nose 3) Ethmoid sinuses- found into the spongy ethmoid bone in the upper part of the nose between the eyes and 4) Sphenoid sinuses- found into the sphenoid bone which is behind the nose between the eyes.

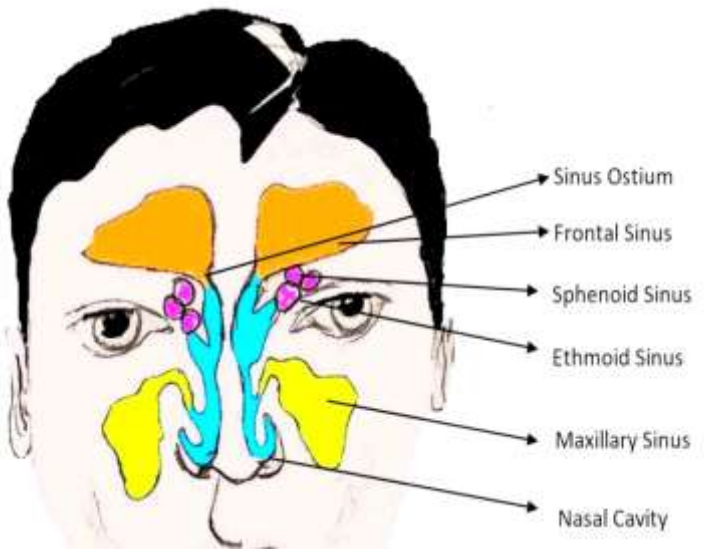

Fig.01 Location of four pairs of sinuses

In present research, 'frontal sinuses' along with their innovative treatment to treat the inflammation caused into them are focused. Frontal sinus is a type of paranasal sinus consisting of a hollow cavity in the bones around the nose. There are total two large frontal sinuses in the frontal bone, which forms the lower part of the forehead and reaches over the eye sockets and eyebrows. The frontal sinus surge lot comprises anatomically of narrow channels inclined to stenosis. Following both endonasal and outside approach, medical surgery into 30% of patients experiences post-operative re-stenosis of the front facing sinus outflow tract, with intermittent frontal sinus disease.

Self - expanding devices are valuable in keeping up with opening or widening bodily structures like veins, arteries, ureters, urethras, hollow body organs, nasal passages, sinus cavities, etc. Implanting or deploying such self expanding devices can expand bodily cavities which is desirable in widening of them. Specifically, self-expanding devices that might offers worthwhile physical as well as practical attributes would be desirable. Furthermore, delivery devices for delivering self - expanding devices and other implants would be alluring.

In our present invention, an idea about a self-expanding bioresorbable scaffold system with its framework and technique in the field of local drug conveyance has been depicted to treat paranasal sinus conditions. More specifically, the treatment of paranasal sinus irritation or inflammation and rhino-sinusitis has been depicted. The strategy for fostering this device has been portrayed in detail. To treat this, a drug eluting bioresorbable sinus scaffold has been designed. Here, the device is composed of a biodegradable material which is kind of a co-polymer. It is designed by keeping its size and shape in consideration at the time of scaffolding. Here, the device has been coated with a specific drug and eluting or release of the drug into the sinuses is controlled by an inactive ingredient that diminishes the time expected for the process as well as the solution required for it. Drug release is slower which is under control of an inactive ingredient, so that it can be effective for a longer period of time. The combination of polymer and drug used to foster the scaffold has shown great importance due to their biochemical property. The device is made of a biodegradable material and it will degrade over its time prior to dissolving.

Materials and Method:

Self-expanding devices are applicable in a variety of locations inside the body as per its requirement to expand or dilate the body cavities. The present research focuses on the frontal sinus and idea of locating a bioresorbable scaffold device to treat the sinusitis. In order to deliver the implant at target site, the delivery system and loaded implant are introduced through the nostrils and directed towards the frontal sinus cavity's ostium (shown in fig. 01) which is visible through the endoscope. As the surgery is carried out through nostrils, it does not alter the outwards contour of the nose or leave any facial scars. The frontal sinus is located in the front part of the forehead that has the shape resembling to a star which requires a device having a comparative profile that can undoubtedly be implanted into the location site of it. Therefore, implantation of the device should be according to the frontal sinus cavity area.

The device is made by hand braiding technique through a mold by maintaining its grip and shape that frames the complete device in a shape of a star which aids in having grip at the location site and allowing the device to crimp without causing any damage to device's structure. The intersection point shown in the fig.01 at the midsection of the braided device were attached by the means of adhesive prepared by dissolving Poly Lactic co-glycolic Acid (PLGA) material in acetone-HPLC grade solution (acts as an adhesive material) generally used to glue the substrates.

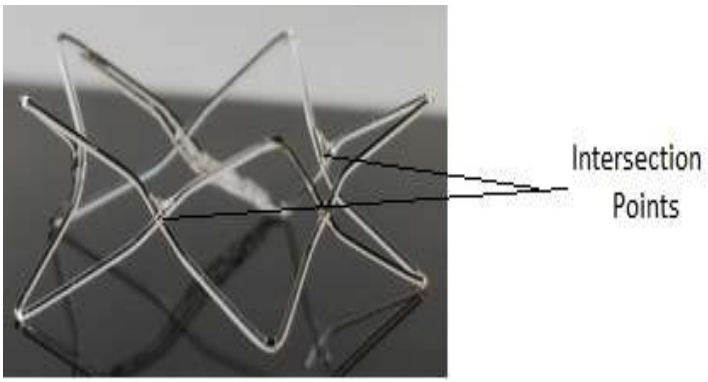

Fig.02 Hand braided (uncoated) device resembling star shape appearance having intersection points.

The device utilized here is made up of a biodegradable co-polymer. As the polymer used is biodegradable; the device will degrade within a pre-determined time of a material utilized. The material used for this application is poly (L-lactide-co-glycolide) PLG (purchased from Durect Corporation)in which 10% is of Lactide & 90% is of co-glycolide that is coated with a drug (active ingredient). This drug is configured utilizing different polymer and inactive ingredients to make its release in order to fulfill its satisfactory purpose. The drug coated with a layer of PLG biodegradable co-polymer of 16-20 µm thickness, which is incorporated with Polyethylene glycol-PEG-6000 (purchased from Sigma Eldrich) of 15µg MF/cm2 of total surface area which is an anti-inflammatory agent used to reduce the swelling of the sinus. The drug used is a mometasone furoate USP (purchased from Coral Drugs pvt. Ltd). It is chosen as it is a hydrophobic drug which is stable under aqueous acidic and oxidative conditions that is similar to body's inner environment, the rate of drug release into the sinuses is controlled by an inactive ingredient polyethylene glycol (PEG-6000). It is utilized as it is a biocompatible, amorphous, biodegradable co-polymeric polymer and hydrophilic polyether compound that easily emulsifies into the solvent medium.

The solvent medium utilized here to dissolve all these ingredients is acetone as it has an ability to dissolve polar as well as non-polar substances and it also evaporates upon specific time and do not cause biochemical changes with the compounds present in the medium. The device made is fixed in spray coating machine that turns the coating solution into a mist and spray it onto the device's surface such that, it favours uniform and sufficient amount of drug coating. A coated device is shown in the fig.02. The fixture is made in such a way that, the fixed device is given only a single degree of freedom to rotate in circular movement in one plane. The device portrayed in this research is only for the frontal sinus cavity.

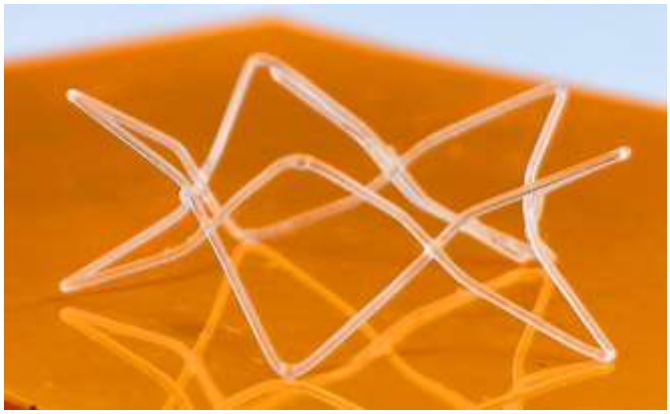

Fig.03 Drug coated device

Result and Discussion:

In the present research, the *in-vitro* release of mometasone furoate USP drug studied using orbital shaker at 37 ℃ through an accelerated HPLC (High Performance Liquid Chromatography) release rate assay. The above mentioned device is made by using a bio resorbable co-polymer poly(L-lactide-co-glycolide) (PLG) by keeping the ratio of lactide and glycolide in 10:90 proportion respectively. Acetone as a solvent medium is used to form a drug coating solution that contains PLG 50:50 and PEG-6000 along with the drug Mometasone furoate USP in it. Total two drug coating solutions were prepared during HPLC performance to check the drug release rate assay: one containing PLG, PEG-6000 and MF drug into the solvent medium, another solution containing PLG and MF drug and not PEG-6000.

It was observed that, the device coated with the solution containing PEG-6000 degraded within 30 days on gradual release of the drug and the device coated with the solution without containing PEG-6000 degraded within 24 hrs. Statistical data of HPLC presented in the Fig.03 illustrates the release pattern of the drug from both the formulations. Total 370 µg of drug was formulated to be coated on the whole device's surface which would gradually elute with time. When drug solution without PEG-6000 was coated on the surface, 100% drug was released within 1 day from the device's surface which was considered in-effective. And, when the drug solution was coated on the device's surface with a PLG 50:50 and PEG 6000

formulation, 20.47µg, 77.18µg, 78.9µg, 107.37µg, & 75.78µg of drug was released on 1st, 7th, 15th, 25th & 30th day respectively.

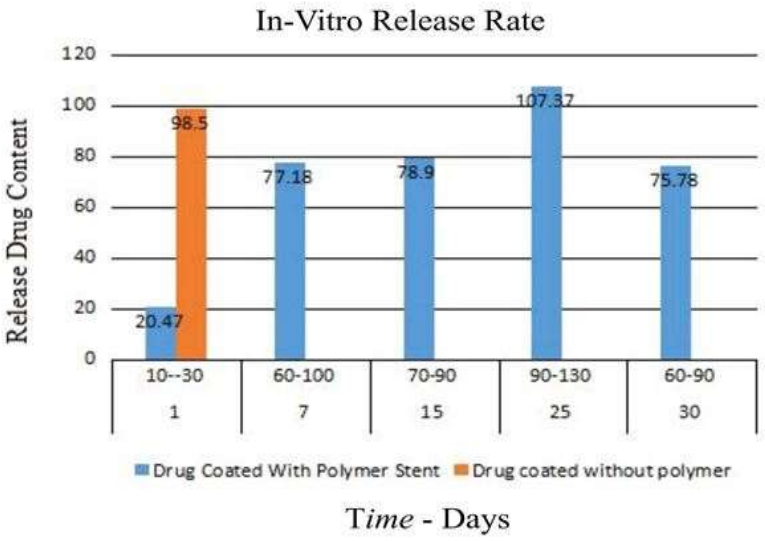

Fig.04: Statistical analysis of HPLC illustrating release pattern of the drug in respective period of time.

Conclusion:

In the present research study, the device portrayed is coated with a layer of PLG biodegradable co-polymer of 16-20 µm thickness, which is incorporated with PEG-6000 of 15µg MF/cm2 of total surface area. PLG & PEG-6000 co-polymers are used as a diffusion barrier from which PEG-6000 acts as a vehicle for controlled release of the drug. It is designed in such a way that, approximately 80% of the total dose of an agent is released in 4 weeks and remaining course in the next 1 week. Hence, through the present research study, it can be indemnified that, the aforementioned drug coated self-expandable bioresorbable sinus scaffold device is relevant as well as promising to treat sinus inflammation within 30 to 45 days of drug release.

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