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MICROSPONGE BASED DRUG DELIVERY SYSTEM: A FUTURISTIC APPROACH IN DISEASE DIAGNOSING AND MANAGEMENT

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Abstract
A medication delivery technology called a microsponge has the adaptability to load a variety of active chemicals because of its huge surface area. It lowers systemic exposure and negative effects and enables the regulated release of active substances. Microsponges are polymeric sponges with flexible, porous structures made of interconnected gaps. With fewer negative effects, microsponge administration systems offer increased product stability, safety, formulation flexibility, effectiveness, and aesthetic appeal. Due to minimal bacterial contamination and the lack of preservatives in the recipe, it is regarded as safe. As a result, it is utilised in several sterile formulations, including ophthalmic and parenteral. This study gives a general overview of the microsponge technology, including its technique, mechanism, programmed release, characterisation, and latest information on formulations that have been commercially successful, their uses, and a list of patents. It also evaluates and applies microsponges in diverse contexts. Although lately utilised for oral applications as well, microsponge is frequently employed for topical applications.

Keywords: Drug delivery, Controlled release, Stability, Biodegradable, Non-toxicity

1. Introduction

In order to alter and regulate the drug's release behavior, novel microsponge-based drug delivery systems have received a lot of attention in recent years. Drugs' therapeutic index and duration of action can be altered through incorporation into a carrier system [1]. The widespread use of ingredients like -hydroxy acids and vitamins in topical products, which can induce perceivable and demonstrable benefits particularly in aging or photodamaged skin has fostered the ever-increasing consumer interest in skin care and treatment products. Despite their usefulness, many of these ingredients may cause irritation; this irritancy is especially common in people who have sensitive skin and manifests as burning, stinging, or redness [2]. Perceiving this issue, the formulators have endeavoured to manage this issue in one of the two techniques. They have decreased the convergence of such fixings, yet all the while, forfeited adequacy [3]. They have also changed the vehicle to make the product more skin-friendly or emollient. However, this method often reduces

the good effects of the finished product. Alternative drug delivery methods and devices are needed because of the expanding field of emerging drugs, increased sensitivity to clinical outcomes, and rising healthcare costs [4]. Drug conveyance frameworks that can exactly control the delivery rates or target medications to a particular body site gigantically affect the medical care framework. A few unsurprising and solid frameworks been created for foundational drugs under the heading of transdermal conveyance frameworks (TDS) involving the skin as a gateway of entry [5]. It has worked on the viability and wellbeing of many medications that might be better directed through skin. However, materials whose ultimate target is the skin itself cannot be delivered using TDS [6]. An area of research that has only recently been successfully addressed is controlled drug release onto the epidermis with the assurance that the drug remains primarily localized and does not enter the systemic circulation in significant quantities [7]. For controlled and localized drug delivery into the stratum corneum and underlying skin layers without going beyond the epidermis, no effective vehicles have been developed. Additionally, the application of topical medications is fraught with numerous issues, such as ointments that are frequently unappealing to the eye, greasiness, stickiness, and so forth, all of which frequently lead to a lack of patient compliance [8]. Due to their poor delivery system, these vehicles necessitate high concentrations of active agents for effective therapy, causing significant users to experience irritation and allergic reactions. The uncontrolled evaporation of the active ingredient, the unpleasant odour, and the potential incompatibility of the drugs with the vehicles are additional disadvantages of topical formulations [9-10]. The purpose of conventional topical drug formulations is to treat the skin's outermost layers. These kinds of products typically release their active ingredients upon application, resulting in a highly concentrated layer that is quickly absorbed. As a result, a system that minimizes an active ingredient's transdermal penetration into the body and maximizes its time spent on the skin surface or within the epidermis is required. Microsponges are minuscule circles equipped for retaining skin emissions, thusly lessening slickness and sparkle from the skin [11]. Round particles made out of groups of considerably littler circles are fit for holding multiple times their weight in skin emissions.In essence, microsponges are sponges at the micro level. It is a polymeric structure with porous microspheres that can hold active ingredients inside [12]. It is a polymeric delivery system that has been patented and is capable of entangling a variety of active ingredients, including sunscreens, emollients, fragrances, essential oils, anti-infective, anti-fungal, and anti-inflammatory agents. Like a typical wipe, it comprises of a horde of interconnecting voids inside a non-folding design, with a huge permeable surface [13]. The size of the microsponges differ, from 5 - 300 μm in distance across, contingent on the level of perfection or after-feel expected for the end equation. A common 25 μm circle can have up to 250000 pores, giving a complete pore volume of around 1 ml/g. Each microsponge gets a big reservoir like this, which can hold as much active agent as it weighs [14]. Because the microsponge particles are too big to be absorbed by the skin, this treatment is non-invasive. The majority of bacteria of the average size range are unable to enter the microsponges' tunnel structure because the pore diameter is smaller.Microsponge particles do not penetrate the skin and are extremely small, inert, and unbreakable spheres [15]. Rather, they gather in the minuscule little hiding spots of the skin and gradually discharge the entangled medication, as the skin needs it. The epidermis and dermis can be protected from an excessive build-up of ingredients thanks to the microsponge system. The microsponge system may be able to significantly reduce the irritation caused by effective medications without compromising their efficacy [16]. The subsequent cleansing then removes the empty spheres. These requirements are met by the microsponge delivery system, which has led to a new generation of novel products that are well-tolerated and highly effective. These items have a relatively high concentration of active ingredients and are typically sold to customers in conventional forms like creams, gels, or lotions. Microsponge are patented polymeric delivery systems made of porous microspheres that can hold a wide variety of active ingredients, including sunscreens, emollients, fragrances, essential oils, anti-infective, anti-fungal, and anti-inflammatory agents [17-19]. Just like a real sponge, each microsphere has a lot of interconnected voids inside of a structure that doesn't collapse and has a big porous surface. Won developed the microsponge technology in 1987, and Advanced Polymer Systems, Inc. received the

initial patents. This company developed numerous variants of the method and applied them to cosmetic, over-the-counter (OTC), and prescription pharmaceutical products [20]. Cardinal Health, Inc. has been granted a license to use this intriguing technology in topical products at this time. Depending on the level of smoothness or after-feel required for the final formula, the microsponges can range in size from 5 to 300 m. Albeit the microsponge size might differ, a run of the mill 25 µm circle can have up to 250000 pores and an inner pore structure identical to 10 ft. long, giving a complete pore volume of around 1 ml/g [21]. As a result, each microsponge has a large reservoir that can hold up to its own weight of active agent. Because the microsponge particles themselves are too big to be absorbed by the skin, these microsponge materials are safer. The possibility of bacterial contamination of the materials entrapped in the microsponge is another safety concern. Bacteria with diameters between 0.007 and 0.2 m are unable to enter the microsponges' tunnel structure because the pore diameter is smaller [22].

2. Microsponges & Current Scenario

Microsponges gain numerous appealing attention from the day of its existence and various companies successfully developed varieties of drug delivery system based on microsponges for numerous disease management and disease diagnosing some of the patents which are produced by the various companies are listed below in **table 1**

Table 1: illustration of various microsponges based drug delivery patents and their numbers

S. No.	Patent Name or Product	Patent Number
1	Weighted microsponge for immobilizing bioactive material	WO/1986/005811
2	weighted microsponge	1275955
3	Weighted microsponge for immobilizing bioactive material	US5100783
4	Methods of fabricating microsponge deuterated hydrocarbon polymer targets which emit neutrons when irradiated by high energy beams	4092381
5	Weighted microsponge for immobilizing bioactive material	0217917
6	Weighted collagen microsponge for immobilizing bioactive material	4863856
7	Weighted collagen microsponge	1288370
8	weighted collagen microsponge for immobilizing bio-active material	US4997753
9	Weighted microsponge for immobilizing bioactive material	1986056694
10	Weighted collagen microsponge for immobilizing bioactive material	4861714

2.1 Characteristics of Microsponges

Microsponge required less mobility's and cost economic technique for its fabrication and development using verities of polymer, enzymes, lipids and other constituents which possess their own native features**(Table 2)**. The following are the main characteristics of the microsponge delivery system:

a) Due to its average pore diameter of 0.25 um, which prevents microbes from entering, microsponge is self-sterilizing and does not necessitate the addition of preservatives to the formulation.
b) It is thermally stable up to 130^{o}C.
c) When compared to other methods of drug delivery, microsponges are less expensive.
d) It works well with most additives and vehicles.
e) Despite remaining as a superfine, free-flowing powder, microsponge have a high payload capacity (50-60% by weight).
f) It is useful for oil control because it can absorb oil six times its weight.
g) Ability to create novel product shapes.
h) Stabilize chemical, physical, and thermal processes better [23-25].

2.2 Drug encapsulation requirements by Microsponges

For fruitful ensnarement of dynamic drug specialists inside microsponges, certain states of the dynamic drug specialists should be reached.The following are the main drug and APIs which are widely utilized in the microsponge drug delivery system**(Table 2)**:

a) It ought to be completely soluble in the monomer, or it should become soluble when a small amount of a solvent that is insoluble in water is added.
b) Monomer latency should be illustrated.
c) It must be water-insoluble.
d) During the formulation, the mixture's viscosity should not be increased.
e) It probably restricted solvency in vehicle for keeping away from restorative issues.
f) The microsponge's spherical structure must be preserved.
g) It ought to remain stable regardless of the polymerization conditions or catalyst.
h) Half-existence of the Programming interface ought to be ought to be under 5hrs to give supported activity.
i) The drug should have a molecular weight of less than 600 g/mol for easy penetration.
j) Plan of polymer and payload of medication should be improved to get wanted discharge rate for a predefined time frame period.
k) In the vehicle, only 10-12%w/w microsponge should be used. Prior to application, the vehicle's microsponge will be reduced if this concentration is not obtained.
l) Due to their solubility or miscibility with an external phase, the microsponge can incorporate both hydrophilic and hydrophobic polymers. Only hydrophilic polymers can be used because of the technology's advantages [26-28].

2.3 Advantages of microsponges based drug delivery system

The basic advantages of microsponges based drug delivery system are ss follows:

a) Microsponges improve the bioavailability of active pharmaceutical ingredients and reduce toxicity while also improving drug solubility and stability.
b) Microsponges Improves item execution.
c) Microsponges support the arrival of medicaments and surrenders constant activity to 12hrs.
d) They have High surface region so higher entanglement productivity.
e) Non-toxic, hypoallergenic, and free of irritants, microsponges are available.
f) Improved thermal, chemical, and physical stability is possible.
g) The creation of new product forms is a simple and quick process.
h) Medication can be straightforwardly applied to target organs.
i) Capability to give the skin a shiny appearance by absorbing oily skin secretions there Material processing is more effective.
j) The immiscible product can be easily snagged by the microsponge [29-31].

Table 2: List of various polymers and drug /APIs used in microsponge based drug delivery system

S. No.	Polymer	Drug/API
1	HPMC	Prednisolone (Corticosteriod)
2	Carbopol 940	Trolamine (Analgesic)
3	Propylene glycol	Acetazolamide
4	Ethyl cellulose	Itraconazole (Anti-fungal)
5	Eudragit L100	Indomethacin (NSAID)
6	Eudragit RSPO	Mupirocin (Anti-Bacterial)
7	Eudragit S 100	Mometasonefuroate (Corticosteriod)
8	Carbopol 934	Erythromycin (Anti-biotic)
9	Eudragit EPO	Retinol (Vitamin – A)
10	Sodium alginate	Lornoxicam (NSAID)
11	PHEMA	Acyclovir sodium (Anti-viral)
12	Acrylic polymers	Benzoyl peroxide (Anti-acne)
13	Eudragit RS 100	Curcumin (Anti-inflammatory)
14	Eudragit RL 100	Diacerein (Anti-bacterial)
15	Polystyrene	Trolamine (Analgesic)

3. Methods of preparation

The various method of microsponges' preparation are as follows **(Figure 1):**

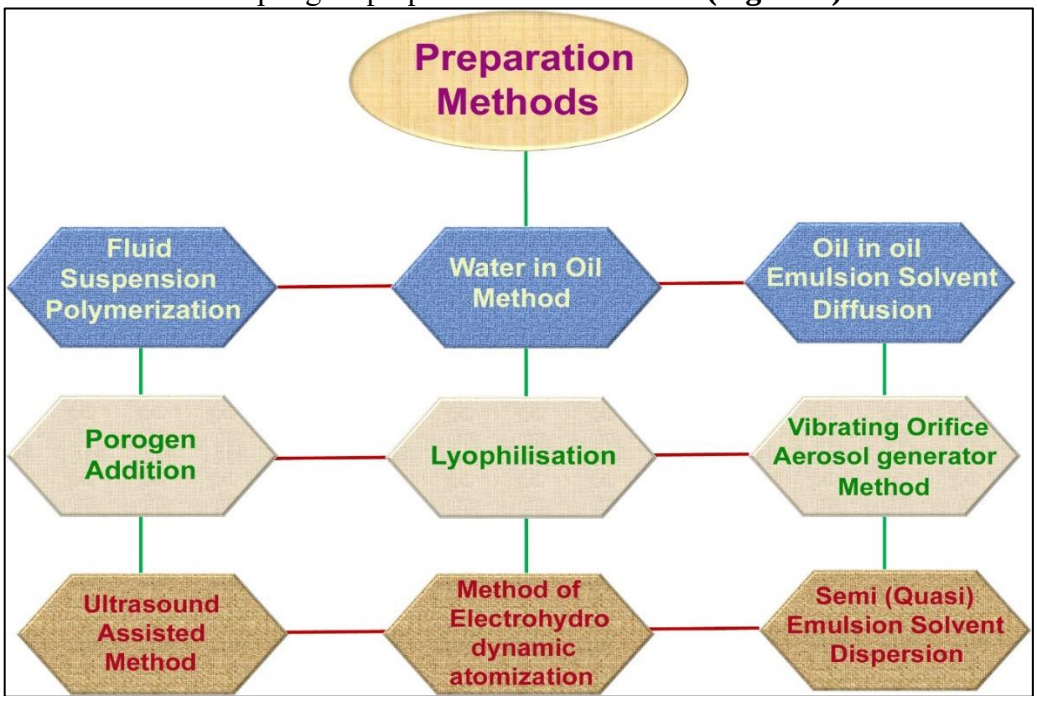

Figure 1: Various method of Microsponges preparations

A. Fluid suspension polymerization

By and large, an answer is made involving monomers and the practical or dynamic fixings, which are immiscible with water. After that, agitation is used to suspend this phase in an aqueous phase that typically contains additives like surfactants and dispersants to aid in suspension. Polymerization is accomplished by activating the monomers through catalysis, elevated temperature, or irradiation once the suspension has been established with discrete droplets of the desired size [32]. As the polymerization interaction proceeds, a round structure is created containing large number of microsponges grouped together like grapes, shaping interconnecting supplies [Figure. The solid particles produced by the process are extracted from the suspension once the polymerization process has been completed. The particles are then washed and handled until they are considerably prepared for use. Starting materials for the microsponge products include methyl methacrylate and ethylene glycol dimethacrylate or styrene and divinylbenzene [33].

B. Semi (Quasi) emulsion solvent dispersion

To set up the internal natural stage, Eudragit RS 100 is broken down in ethyl liquor. Then, the medication is added to the arrangement and broke up under ultrasonication at 35^{o}C [34]. The internal stage is filled the polyvinyl liquor arrangement in water (external stage). The mixture is filtered to separate the microsponges after 60 minutes of stirring. Ingredients can be entrapped in microsponge polymers either at the time of synthesis or, if they are too labile to withstand polymerization conditions, they can be post-loaded after the microsphere structure has been pre-formed. The microsponges are dried in an air-heated oven at 40 degrees Celsius for 12 hours. As a rule, the last option process is the favoured mode, as numerous restorative fixings, and most drug ones, would deteriorate at the temperatures utilized for polymerization [35].

C. Water in oil method

Using this method, an internal aqueous phase containing an emulsifying agent was dispersed in an organic polymeric solution for an oil-in-water emulsion. To create a double emulsion, this oil emulsion's water was once more dispersed in an external aqueous phase containing PVA. In this technique both water-dissolvable and water insoluble medications can be ensnared [36].

D. Oil in oil emulsion solvent diffusion

The emulsion was prepared using this method because the internal phase is a volatile organic liquid. Dichloromethane is the volatile solvent of most preparations. Additionally, span 85 external phase polyactide glycolic acid is the polymer used in this. The inside stage was added to the scattering medium in dropwise with consistent blending to get the microsponge [37].

E. Porogen addition

To accomplish this, porogen, such as sodium bicarbonate or hydrogen peroxide, is added to the internal phase. The porogen was redispersed in the PVA-containing aqueous phase after being distributed uniformly throughout the polymeric solution. The addition of hydrogen peroxide has the effect of creating pores that are interconnected and have diameters ranging from 5 to 20 micrometers [38].

F. Lyophilisation

By quickly removing the solvent, lyophilization transforms the microspheres into porous microspheres, resulting in porous microspheres. Using a solution of chitosan hydrochloride, this is done. After being lyophilized, the microspheres are incubated in this solution. Due to the rapid removal of the solvent, microparticles may shrink and crack [39].

G. Vibrating Orifice aerosol generator method

The preparation of lipid bilayeredmesoporous silica particles was the primary application for the vibrating orifice aerosol generator method. Tetraethylorthosilicate, ethanol, water, and diluted hydrochloric acid were refluxed to create the stock solution for the core particle. After being diluted with the surfactant-containing solvent, this solution continued to form monodisperse droplets [40]. The lipsomes contain the newly formed microspheres. 8] For the preparation of the microsponge, these are the few reported methods. The above strategies have its all own different method of readiness, From this the greater part of the microsponges are ready by utilizing Semi Emulsion Dissolvable Dispersion, contrast and different techniques semi emulsion dissolvable dissemination has least inconveniences for the pre-arranged item [41].

H. Ultrasound-assisted method

This method modifies the polymerization of a liquid-liquid suspension. Microsponges are delivered by utilizing monomers and cross-connecting specialists. Beta-cyclodextrin serves as the monomer, while diphenyl carbonate serves as the cross linker [42]. The subsequent combination was permitted to cool in the wake of warming and sonication. From that point onward, permeable, sporadic microparticles were made by squashing the resultant item. The main advantages of this system is there are no solvent traces, and the outcomes are consistently and quickly achieved. Disadvantages: Remaining toxic cross-linking agents become entangled; unpredictable construction might result [43].

I. Method of electrohydrodynamic atomization

The porous chitosan microspheres were produced using this technique. The chitosan arrangement was held for sonication to create bubbles. After that, the suspension was electro-hydrodynamically atomized, perfused through a capillary, and placed in a syringe. Ion-induced gelation was used to create microparticles. The appropriate voltage and flow rate were supplied during setup [44]. In a beaker, the aqueous NaOH solution was made and kept. During the electro spraying of chitosan solution, the electro sprayed chitosan gels are formed when a beaker is placed on a magnetic stirrer and constantly stirred. After an hour, the NaOH solution in which the chitosan droplets collected took on a spherical shape [45].

4. HYPOTHETICAL MECHANISM OF ACTION

An entrapped form of the active ingredient is added to the vehicle. The active is free to move in and out of the microsponge particles and into the vehicle until equilibrium is reached, when the vehicle becomes saturated, due to the open structure of the microsponge particles. When the finished product is applied to the skin, the active that was already in the vehicle will be absorbed into the skin, depleting the vehicle and causing it to become unsaturated, causing the equilibrium to be disturbed [46]. This will initiate a flow of the active from the microsponge particle into the vehicle and through the vehicle to the skin until the vehicle is either dried out or absorbed. Even after that, the active will continue to be slowly released to the skin by the microsponge particles that are still on the stratum corneum's surface, providing a prolonged release over time [47]. The significance of developing vehicles for the treatment of microsponge entrapments is emphasized by this proposed mechanism of action. During the process of compounding the finished products, the active may not provide the desired benefits of gradual release if it is too soluble in the desired vehicle. Instead, they'll act as though the active was just added to the vehicle. As a result, when developing microsponge entrapments, it is critical to develop a vehicle with low active solubilizing power [48]. This rule is in opposition to the ordinary plan standards normally applied to effective items. The active's maximum solubility in the vehicle is typically recommended for these conventional systems. Because the vehicle can provide the initial loading dose of the active until the shift in equilibrium from the polymer into the carrier triggers release from the microsponge, using microsponge entrapments allows for some solubility of the active in the vehicle. Formulating the product with some free and some entrapped active so that the vehicle is pre-saturated is another way to prevent undesirable premature leaching of the active from the microsponge polymer [49]. For this situation there won't be any filtering of the dynamic from the polymer during compounding. In the end, the rate of active release will be influenced not only by the active ingredient's partition coefficient between the polymer and the vehicle (or skin), but also by some of the parameters of the beads. Surface area and, more specifically, mean pore diameter are two examples of these. Release can also be controlled through diffusion or other triggers like moisture, pH, friction, or temperature [50].

5. RELEASE MECHANISM OF MICROSPONGE

Microsponges can be designed to release a specific amount of active ingredients over time in response to one or more of the following external triggers**(Figure 2)** [51].

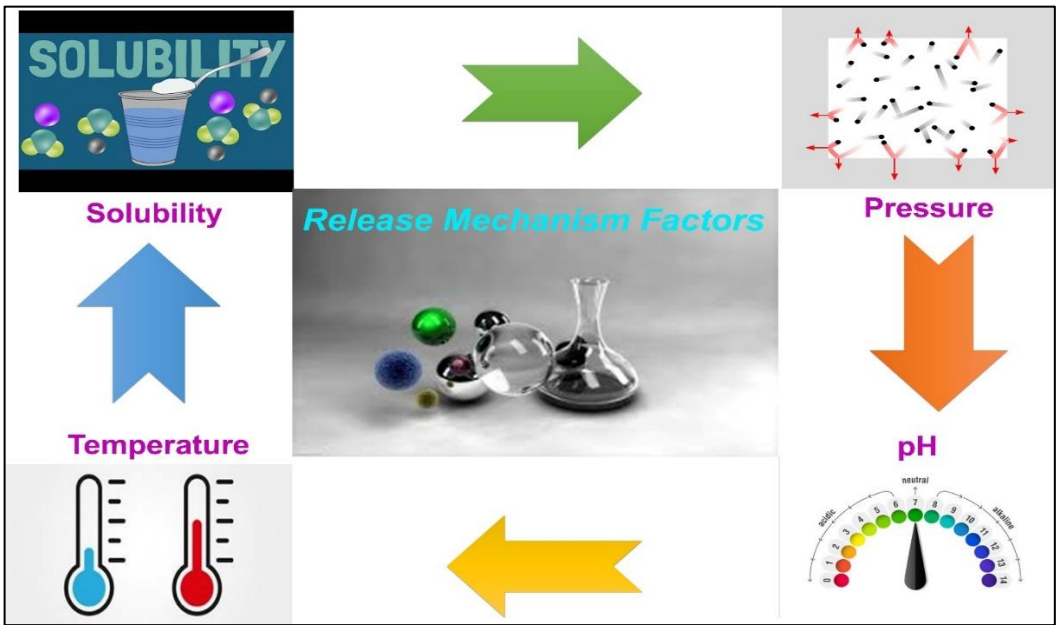

Figure 2: Different factors which influenced the release mechanism of the microsponge delivery system

a. Pressure

Microsponges' active ingredients can be absorbed by the skin through rubbing or applying pressure [52].

b. Solubility

Microsponges stacked with water-dissolvable fixings like antiprespirants and germ-killers will deliver the fixing within the sight of water. Taking into account the ingredient's partition coefficient between the microsponges and the external system, diffusion can also activate the release [53].

c. Temperature variation

A few ensnared dynamic fixings can be excessively thick at room temperature to stream unexpectedly from microsponges onto the skin. Expanded in skin temperature can bring about an expanded stream rate and thus discharge. Franz-type static diffusion cells can be used to study drug release from the topical semisolid formulation [54].

d. pH set off discharge

An adjustment of pH starts drug discharge in this strategy, which is accomplished by changing the covering on microsponges for pH-based actives [55].

6. Microsponge characterization parameters

The different characterization parameters which directly influence the microsponge properties like preparation, drug encapsulation, release and stability are discussed below **(Figure 3)**

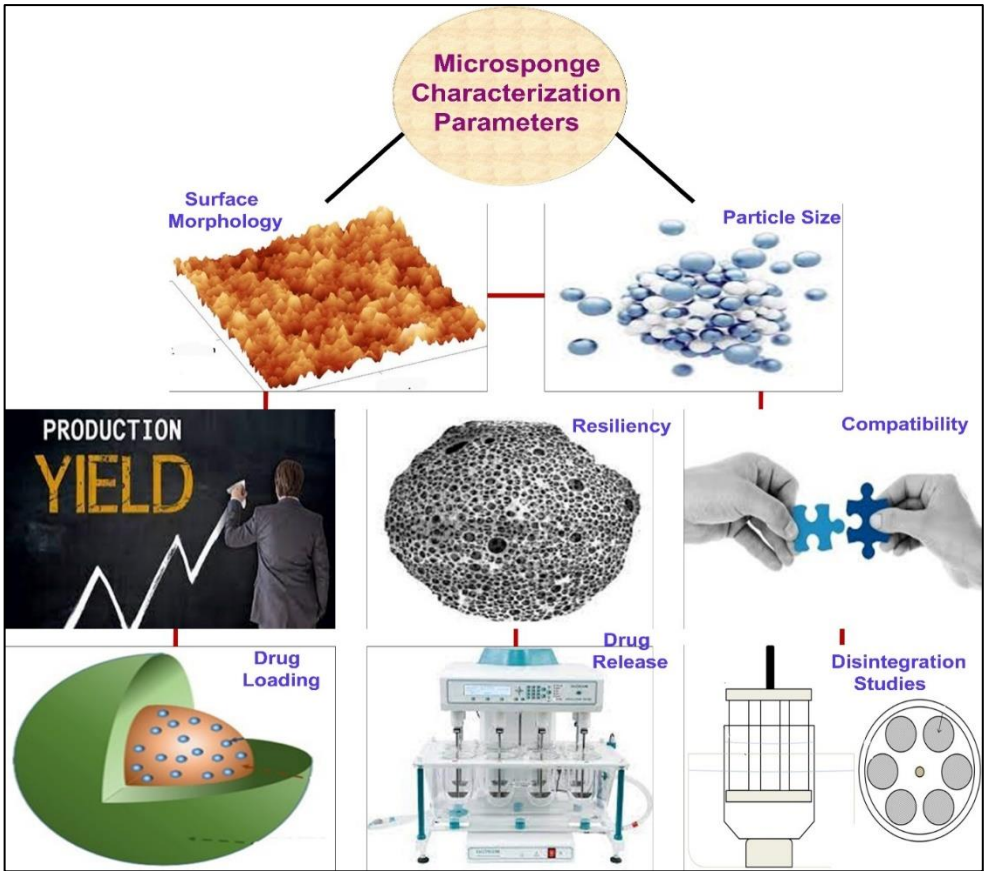

Figure 3: Illustration of Microsponge characterization parameters

a. Particle size

An optical or electron microscope is used to measure the size of microsponges. The performance of the formulation is impacted by the particle's size. Drugs are among the factors that influence particle size: the concentration of the emulsifying agents and the polymer ratio [56]. Particle size decreases as the drug polymer ratio rises, while the concentration of emulsifying agents rises, resulting in larger particles. A calibrated ocular and stage micrometer were used with an optical microscope to

measure the size of the particles. On a clean glass slide, a cover slip is placed over a small amount of microsponges and a drop of liquid paraffin. Each batch's 100 particles were measured to determine the average particle size [57].

b. Production yield

The medication polymer proportion additionally influences creation yield, an expansion in drug: production yield also rises as a result of polymer ratio [58].

Production yield = Practical quantity/Theoretical quantity x 100

c. Loading efficiency

Drug loading in microsponge is determined by the drug's physicochemical properties. Active loading and passive loading are the two modes of drug loading. Most effective is passive loading. A rise in drug use: Increasing the polymer ratio improves drug loading efficiency. The formula for determining the loading efficiency is [59]:

Loading efficiency = Practical drug loading/Theoretical drug loading x 100.

d. Surface topography

Various methods, including scanning electron microscopy (SEM), transmission electron microscopy (TEM), and others, have been utilized in surface topography. The prepared microsponges are frequently examined with SEM [60].

e. In vitro release studies

In vitro release studies are carried out with a modified basket made of 5 m stainless steel mesh and the dissolution apparatus USP XXIII. Under 150 rpm speed, dissolution rates were measured at 37^0C. The active ingredients' solubility is taken into consideration when selecting the dissolution medium. The suitable analytical method was used to extract samples from the dissolution medium [61].

f. Disintegration study

Microsponges in vitro disintegration information is gotten utilizing a changed USP XXIII crate disintegration gadget with a 5um tempered steel network. Dissolution media are selected based on the solubility of the active components, and the temperature is maintained at 37^0C and 150 rpm. The examples are removed from the disintegration media at explicit time stretches and examined utilizing the suitable insightful methodology [62].

g. Resiliency Microsponges'

The viscoelastic qualities (resiliency) can be tweaked to produce softer or stiffer bead lets, depending on the requirements of the final formulations. The various apparatus and media used to analyse the permeation profile and drug release from MS are presented in the table. Dissolving medium selected according to the solubility of active ingredients for maintaining proper sink conditions [63].

h. Studies of compatibility

The drug's compatibility with reaction additives can be determined using Fourier transform infrared spectroscopy and thin layer chromatography (TLC). Differential scanning colorimetry (DSC) and powder X-ray diffraction (XRD) are two methods that can be used to identify the crystallinity of polymer-based medications [64].

7. MICROSPONGE-BASED DRUG TRIGGERING DELIVERY SYSTEMS

The various types of drug delivery system can be employed via microsponges as elaborated in Table 3

a. Topical drug delivery system

Microsponge technology was used for topical drug delivery. An emulsion solvent diffusion method was used to develop microspongic delivery of benzoyl peroxide [65]. An organic internal phase containing benzoyl peroxide, ethyl cellulose, and dichloromethane was added to a stirred aqueous phase containing polyvinyl alcohol and suspension polymerization of styrene and divinyl benzene was used to dissolution of the drug was released at a slower rate in the entrapped system than in the free BPO-containing system [66]. A new formulation of Hydroquinone (HQ) 4% and retinol 0.15%

entrapped in microsponge reservoirs was developed to release HQ gradually, prolong treatment exposure, and minimize skin irritation. The topical delivery system with reduced irritancy was developed successfully. In a 12-week open-label study, this product's safety and effectiveness were evaluated [67]. The microspongic system for topical delivery of fluconazole gel was observed to have the potential to extend the release. An MDS system for retinoic acid was developed and tested for drug release and anti-acne efficacy in this open-label study. When tretinoin was entrapped in the microsponge, there was a statistically significant reduction in both inflammatory and non-inflammatory lesions.Topical analgesics, anti-inflammatory drugs, and anti-irritants are used to treat musculoskeletal solubilisation [68]. Sustained release formulation of chlorpheniramine maleate is prepared for oral drug delivery using powder-coated microsponges. Controlled oral delivery of ketoprofen was prepared by quasi-emulsion solvent diffusion method with Eudragit RS 100, and tablets of microsponges were then prepared using the direct compression method. Sustained release formulation of chlorpheniramine maleate is prepared for oral drug delivery using powder-coated microsponges. The findings indicated that the drug-polymer physical mixture significantly improved compressibility; due to the plastic deformation of the sponge-like microsponge structure, which results in mechanically strong tablets. A commercial Microsponge® 5640 system was used to deliver flurbiprofen in a controlled, colon-specific manner [69-70].

b. Oral drug delivery using microsponge technology

In oral applications, the microsponge system has been shown to increase the rate of solubilisation of poorly water-soluble drugs by entrapping such drugs in the microsponge system's pores [71]. In vitro studies showed that compression-coated colon-specific tablet formulations started to release the drug at the eighth hour, corresponding to the proximal colon arrival time, due to the addition of the enzyme, following a modified release pattern. On the other hand, the drug is effectively reduced to microscopic particles as a result of the extremely small pores, and the significant increase in surface area results in a significant increase in the rate. By combining two aqueous dispersions of a-tricalcium phosphate grains and calcium-deficient hydroxyapatite powders with pre-polymerized powders of polymethylmethacrylate and liquid methylmethacrylate monomer, bone-substitute compounds were created [72].

c. Microsponge-based delivery systems for bone and tissue engineering

The basic fibroblast growth factor (bFGF) that was incorporated into a collagen sponge sheet remained released in the mouse subcutis in accordance with the biodegradation of the sponge matrix and exhibited dose-dependent local angiogenic activity [73]. The final composites appeared to be porous and functioned as microsponges. Intra-strong infusion of collagen microsponges consolidating bFGF, prompted a critical expansion in the blood stream, in the murine ischemic rear appendage, which would never have been achieved by the bolus infusion of bFGF [74]. A biodegradable graft material containing the collagen microsponge was developed for cardiovascular tissue grafting, as it would permit the regeneration of the autologous vessel tissue. A thin biodegradable hybrid mesh of synthetic poly (DL-lactic-co-glycolic acid) (PLGA) and naturally derived collagen was used for a three-dimensional culture of human skin fibroblasts. These findings suggest the significance of the type I collagen as a reservoir of bFGF and a tissue-engineered patch made of our biodegradable polymer and collagen-microsponge provided good in situ regeneration at both the venous and arterial walls, suggesting that this patch could be used as a novel surgical material for the repair of the cardiovascular system [75]. The hybrid mesh was constructed by forming web-like collagen microsponges in the openings of a PLGA-knitted mesh. The oral route is convenient, safe, and non-toxic for administration; however, it has disadvantages such as rapid drug excretion due to a short halflife and significant first-pass metabolism in some formulations [76]. Therefore, various microsponges' plans are produced for controlled and designated oral conveyance, with different purposes. The microsponge's technology increases the rate at which hydrophobic medicines are absorbed by securing them within pores. When the surface area for smaller particles is large, it speeds up solubilisation [77]. By altering the intra-particle density of eudragit RS,

ibuprofen microsponges were made for controlled drug distribution. Using the dry impact mixing method, chlorpheniramine maleate powder coated microsponges are produced for prolonged release. The direct compression method is used to produce ketoprofen microsponges, which are then pressed into tablets for controlled oral administration [78].

Table 3: Illustration of Microsponge based different types of drug delivery system

S. No.	Microsponge Based delivery system	Drug/API	Disease
1	Ocular	Acetazolamide Atenolol	Glaucoma Anti-hypertensive
2	Implants	PLGA	skin tissue engineering
3	Capsule	Curcumin	Anti-inflammatory
4	Gels	Benzoyl peroxide Fluconazole Mupirocin Diclofenac sodium Acyclovir Hydroxyzine HCL Terbinafine HCL	Anti-acne treatment Inflammation Antibacterial activity Inflammation Viral infection Urticaria and atopic dermatitis Anti-fungal
5	Lotion	Benzoyl peroxide	Anti-acne treatment
6	Grafts	PLGA	Cardiovascular surgery
7	Injections	Basic fibroblast growth facto Acyclovir Benzoyl peroxide Diclofenac sodium	Growth factor Viral infections Anti-acne treatment Inflammation
8	Creams	Hydroquinone and retinol	Melanoma
9	Tablets	Indomethacin ParacetamolChlorpheniramine maleate KetoprofenFenofibrate meloxicam	Anti-pyretic Hay fever Musuloskeleton pain Gout Arthritis, Inflammations.

8. Effect of Variable formulation on Microsponges

a. Effect of internal and external phase composition

The apparent viscosity of the dispersed phase was directly proportional to the microsponge particle size. Assuming more distinction between obvious consistency of scattered and nonstop stage, bigger the mean molecule size of the microsponge. At the point when the scattering stage is more gooey is filled the persistent stage (outer stage), the globules of the framed emulsion can scarcely be separated into more modest particles and greater drops are found bringing about an expansion in mean molecule, because of the greater consistency of the inward stage [79]. The best microsponges can only be made with 3 to 5 milliliters of internal phase. Both the drug content and the production yield of microsponges decrease when the internal phase is increased from 5 to 15 milliliters. This is because of the greater grouping of interior stage with lower convergence of medication [80].

b. The ratio of the drug to the polymer

The parameter affected by the drug: Particle size changes with the polymer ratio. The microsponge's particle size increases with the drug's concentration. The loading capacity is not significantly affected when the ratio of the drug to the polymer is varied, but the production yield can change significantly from the minimum ratio to the maximum ratio when the concentration of the polymer remains constant [81].

c. Impact of mixing rate

Microsponges of lesser size are gotten as the mixing rate is raised. The production yield decreases as the stirring rate rises, but the drug content rises, indicating that drug loss decreases as the stirring rate rises. This is because of the choppiness actuated in outside stage, which makes the polymer adhere to the oar and decreases producing yield [82].

9. Delivery of Drugs with the use of Microsponges

A number of anti-ulcer, antimicrobial, anti-cancer, anti-hypertensive, and anti-inflammatory medications are developed with the help of microsponges. These medications are outlined below**(Figure 4)** [83].

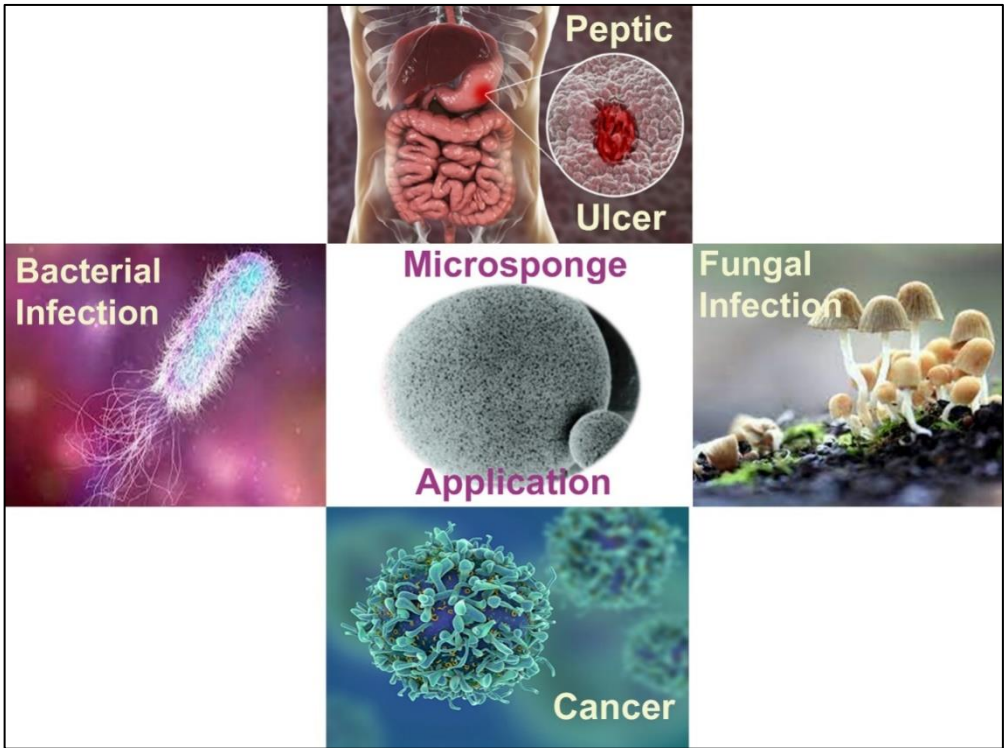

Figure 4: Illustration of Microsponge based drug delivery system in various disease

a. Drugs for Peptic Ulcers

Research fraternity had deeply investigate the use of microsponges to target enteric cells with drugs for peptic ulcers. The topic of this study was gastroretentive microcapsules. As a result, Gandhi et al. developed Resveratrol encapsulated in ethyl cellulose microsponges and Ranitidine hydrochloride encapsulated microsponges [84]. In the treatment of GERD, newer antiulcer drugs embedded in microsponges, such as Cimetidine-encrusted floating microsponges, Pirenzepine-encrusted microballoons, and Omeprazole-encrusted microsponges, have been developed. The successful development of H2 blocker-loaded gastro retentive microsponges that provided sustained drug release at the site of action confirmed the usefulness of microsponges as floating gastro retentive systems [85]. Microsponges' high drug loading capacity made it easy to make them into a traditional capsular system for treating gastric ulcers. These delivery systems have the potential to benefit from enhanced therapeutic response, predictable rate of release, extent of absorption, and improved patient acceptance for scientific and economic reasons [86].

b. Antifungal Medicines

Microsponges are used to make it easier for many hydrophobic substances to be absorbed. It has been discovered that most topical antifungal medications are quite hydrophobic. They created a gel with improved drug delivery for fluconazole-entrapped microsponges, while Mahaparale contemplated the antifungaltherapy of terbinafinemicrosponges. Miconazole was used in the same way by many times. Dermatological infections are treated with hollow itraconazole microsponges. The majority of antifungal medications are formulated as gels or creams that claim to speed up absorption [87]. The microsponges loaded gel had a good drug yield and drug loading capacity, released in a controlled and sustained manner. Topical treatment with fluconazole for serious dangerous skiing parasitic contaminations has demonstrated to be a proficient treatment involving a

high flying situation among the options of treatment. These microsponge gel are expected to remain on the skin for a longer period of time than conventional formulations, gradually releasing their contents over time. As a result, the microsponges and microsponge gel made with oxiconazole nitrate in this study appear to be more effective than standard formulation therapy [88].

c. Anti-bacterial medicines

Mupirocin microsponges, Dicyclomine-loaded microsponges, and Benzoyl Peroxide gel are among the numerous advancements made in microsponges in relation to antibiotics. In surgical wound models infected with S. aureus in mice, emulgel formulations based on microsponges demonstrated prolonged efficacy [89]. Mupirocin was stable in topical emulgel formulations and had better skin retention, indicating that the delivery system had better potential for treating primary and secondary skin infections like impetigo, eczema, and atopic dermatitis. The medical field makes extensive use of antibiotics. Due to bacterial resistance and the ineffectiveness of the preparation, the requirement changes annually [90]. Therefore, it is essential that we have access to a variety of drug delivery systems so that we can adapt to the ever-changing world. Organic antibacterial drugs have undergone significant development in light of more natural products and ingredients. Azadirachtaindica, ordinarily known as the neemplant, and its concentrates have displayed to have antibacterial impacts against different oral microorganisms. In chronic inflammatory lung diseases, oligonucleotide therapy has proven to be an emerging focus area for drug delivery [91].

d. Treatments for cancer

Chemotherapy, radiation, and surgery are the classic cancer treatments of today. However, these treatments have severe mental and biochemical side effects that primarily destroy the patient's healthy cells. Chemotherapeutic drugs are effective against a wider range of cancers, including colorectal cancer, breast cancer, stomach cancer, and skin cancer [92]. The field of anticancer drug delivery is still in its infancy, and numerous delivery systems have been developed for particular types of cancer. For skin cancer, Bhatia et al.'s Curcuminmicrosponges and Curcuminbetacyclodextrin, as well as 5-Fluorouracil for colon cancer, have been developed. The use of enteric-coated HPMC capsules with 5-fluorouracil-loaded microsponges as a dosage form for colon targeting appears promising. Natural products have shown promise as cancer-fighting agents [93]. Carallumafimbriata has been shown to have a strong cytotoxic effect on human colon cancer cells, and numerous new trends in novel drug delivery strategies for the treatment of lung cancer have been discovered, and Acacia catechuethanolic bark extract can kill oral squamous carcinoma cells in humans, Acacia catechuethanolic seed separates against SCC cells, Coumarin subsidiaries have shown anticancer impacts against stomach malignant growth, syringic acid's role in liver cell cytotoxicity, and selenium nanoparticles as a chemotherapeutic agent oxidative stress in chronic liver disease, the antihyperglycemic activity of Carallumafimbriata, and targeted drugs for hepatic fibrosis [94]. Zinc oxide combination utilizing Mangiferaindicaforcellular breakdown in the lungs and so forth. Nanotechnology is a steadily developing field with heaps of chances. Using nanoparticles, there has been a breakthrough every year. Larvicidal activity of Antimicrobial Silver Nanoparticles synthesized using Garciniamangostana Bark Extract and bacteriotoxic activity of Zinc Oxide Nanoparticles synthesized using Brassica oleracea are two of the most well-known antibacterial nanoparticles. All of these recent studies raise the possibility of additional plant-based microsponges for various diseases in the future [95].

e. Miscellaneous

Medication to treat arthritis have identified diclofenac sodium as a treatment for Medication for hypertension found that atenolol entrapped microsponges as well as the topical antibiotics voriconazole, erythromycin, and tretinoin.The human skin is a significant objective site for drug application in dermatological problems. To limit the therapeutic effect, topical drug delivery is preferred for its treatment [96].

10 Marketed Formulations

The microsponges areexcellent for personal care products and skin care. They retain an elegant feel on the skin's surface while absorbing a significant amount of excess oil. The technology is currently used in almost all of the products that major global manufacturers of cosmetics and toiletries sell [97]**(Table 4)**. Skin cleansers, conditioners, lotions to control oil, moisturizers, deodorants, razors, lipstick, makeup, powders, and eye shadows are among these products; which has a number of advantages, including improved chemical and physical stability, increased concentrations that are readily available, controlled release of the active ingredients, less skin irritation and sensitization, and unique tactile qualities. Advertised plan utilizing the MDS incorporates Moral Dermatological items (APS characterized moral dermatology items as solution and nonprescription medications that are advanced principally through the clinical calling for the avoidance and treatment of skin issues or illnesses) [98]. In the United States, a number of over-the-counter (OTC) and personal care products that have been approved by the US Food and Drug Administration are sold. Multiple human clinical studies demonstrated that the technology has the potential to reduce drug side effects, maintain therapeutic efficacy, and possibly boost patient treatment regimen compliance [99].

Table 4: Elaboration of some Microsponges based important marketed product

S. No.	Product	Company	Application
1	Carac Cream	Dermik Laboratories, Inc. Berwyn , PA 19312 USA	In actinic keratosis
2	Retin A Micro	Ortho-McNeil Pharmaceutical, Inc.	In Acne Vulgaris
3	EpiQuin Micro	SkinMedicaInc	In melasma, post inflammatory hyper pigmentation or solar lentigines
4	Salicylic Peel 20 & 30	Biophora	In hyperpigmentation, acne and inflammations.
5	Micro Peel Plus /Acne Peel	Biomedic	In dead skin peeling, inflammations and acne
6	Lactrex™ 12% Moisturizing Cream	SDR Pharmaceuticals, Inc., Andover , NJ ,	Act as natural humectant, to soften and help moisturize dry, flaky, cracked skin.
7	Ultra Guard	Scott Paper Company	It help to protect a baby's skin from diaper rash
8	Aramis fragrances	AramisInc	Antiperspirant Spray
9	Dermalogica Oil Control Lotion	John and Ginger Dermalogica Skin Care Products	It help to reduce oily shine on skin’s surface.
10	Sportscream RS and XS	EmbilPharma. Ltd.	Topical analgesic-anti-inflammatory and counterirritant cream

11. Conclusion and Prospects for the Future

The microsponge delivery system is a one-of-a-kind method for the controlled release of macroporous beads loaded with active agent. It has the potential to reduce side effects while still maintaining the therapeutic efficacy of the beads [100]. It is thought that the microsponge drug delivery system helps reduce side effects, improve stability, make products look better, and make them more flexible in their formulations by entangling their components. Furthermore, numerous studies have demonstrated that microsponge systems are non-toxic, non-mutagenic, and non-irritating. This innovation is being utilized presently in beauty care products, over-the-counter healthy skin, sunscreens, and solution items [101]. The treatment of a number of diseases may be better understood with the help of this kind of drug delivery technology. As a result, the microsponge-based drug delivery technology has a good chance of becoming a useful drug delivery matrix substance in the future for a variety of therapeutic applications. One of the novel drug delivery systems, microsponges, were initially developed for topical drug delivery [102]. They can

likewise be utilized for tissue designing and controlled oral conveyance of medications utilizing biodegradable polymers. It gives an extensive variety of forming benefits. Powders that flow freely can form from liquids. Without the use of preservatives, formulas can be made with ingredients that are otherwise incompatible and remain stable for an extended period of time. When it comes to formulations like the transdermal delivery system, microsponges will therefore be an ideal drug delivery system. Significant users experience irritation and hypersensitivity reactions due to the fact that it necessitates vehicles with a higher concentration in order to dissolve the API for effective therapy [103-104]. One more bad mark of skin plans is uncontrolled dissipation of the captive fixing, upsetting scent, and the expected contradiction of medications with the vehicles. Ordinary plans of skin drugs are planned to chip away at the external layers of the skin. Commonly, such items discharge their dynamic fixings upon application, creating a profoundly thought layer of a functioning fixing that is quickly consumed. As a result, a method to extend the amount of time an active ingredient stays in the epidermis or on the skin's surface is needed. Some microsponge-based items are now endorsed; several more are currently in the process of clinical evaluation and development [105].

11. Conflict of Interest

The author declares no conflict of interest

12. Acknowledgement

13. References

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