

## FORMULATION, DEVELOPMENT AND EVALUATION OF MUCOADHESIVE PATCHES FOR BUCCAL DRUG DELIVERY SYSTEM

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### ABSTRACT

The utilization of mucoadhesive medication conveyance frameworks is a promising development in the field of drugs. Mucoadhesive medication conveyance frameworks are especially applicable for getting neighborhood and foundational drugs dissemination in the Gastro Digestive system (GIT) for a delayed timeframe at a foreordained rate. This is rather than oral controlled discharge drug conveyance frameworks, which are many times subject to broad presystemic digestion and corruption in the acidic climate of the stomach, bringing about lacking assimilation of the medications. One of the benefits of mucoadhesive medication conveyance frameworks is that they consider direct section of medicine into the fundamental flow through the buccal mucosa, which is the covering of the mouth. This outcomes in simple organization without torment, brief enzymatic action, less hepatic digestion, and higher bioavailability of the drug. Furthermore, mucoadhesive medication conveyance frameworks don't need broad patient consistence or management, as is much of the time the case with parental medication conveyance systems. The instrument of mucoadhesion includes the cooperation between the mucoadhesive polymer and the bodily fluid layer of the mucosal surface. Mucoadhesive polymers are intended to stick to the mucosal surface and stay set up for a drawn out timeframe, considering a supported arrival of the medication. In-vitro and in-vivo mucoadhesion testing procedures are utilized to assess the adequacy of the mucoadhesive medication conveyance system. In outline, mucoadhesive medication conveyance frameworks offer a few benefits over conventional oral controlled discharge and parental medication conveyance frameworks, including higher bioavailability of the medication, simplicity of organization, and supported discharge. Further exploration is expected to advance the plan of mucoadhesive medication conveyance frameworks and to completely comprehend their possible in the field of pharmaceuticals. Catchphrases: Buccal medication conveyance framework, Mucoadhesive medication conveyance framework, Mucoadhesion, mucoadhesive polymers, Penetration enhancers, Bioadhesive.

**KEYWORDS:** Buccal, Films, Gums, Patches, Therapeutic efficacy, mucoadhesive polymers, Permeation enhancers.

### INTRODUCTION

The advancement of the measurement structure occurred not by some coincidence but rather by need. The created measurements structure ought to address the issues of the patient and act productively, steady and affordable and discharges the medication to the wanted area with least aftereffects.<sup>[1]</sup> Prior there were regular measurement frames that were ready however as of late they were supplanted with NDDS, these produced positive results by expanding the existence of the medication. Now NDDS isn't simply hypothesis, broad work is happening in all potential ways where it tends to be appropriate and profitable, one among them is buccaladhesive medication conveyance framework.<sup>[2,3,4]</sup> There were many courses by which the NDDS can be controlled however most favored is oral course as a result of its high pace of

worthiness and reproducibility. There were even a few difficulties for oral course however these were not as much affected during the peculiarities of medication discharge.

### Buccaladhesive Drug delivery

The excellent elements of oral mucosa make it a doable site for supported discharge conveyance frameworks, which could keep a consistent arrival of medication in the fundamental dissemination.<sup>[5]</sup> Different conveyance approach have been formed to convey drugs into the oral hole for one or the other nearby or foundational activity. These incorporate mouthwashes, capsules, gels, biting gums, candies, patches, transmucosal device and some particular tablets.<sup>[6]</sup>

The simple and most traditional doses are tablets and mouthwash. The drug is continually washed away by a lot of spit from these non-joined conveyance frameworks coming about into beginning burst impact followed by a fast lessening in focuses to beneath restorative levels.<sup>[7]</sup> Also, the measurement structure should be satisfactory for a superior patient consistence. In like manner, standard gels, glues and even measurements structures for supported discharge through buccal mucosa<sup>[8]</sup>, for example, cured biting gums, sedated candies and capsules couldn't defeat the salivary rummaging impact. To conquer these limits, conveyance frameworks intended to stay in the buccal mucosa for delayed period in light of the idea of bioadhesion/mucoadhesion has been created.<sup>[9]</sup>

### BIOADHESION

It is the peculiarity where an engineered or regular macromolecule sticks to a natural tissue, which can be an epithelial surface or a bodily fluid layer covering a tissue, and is kept intact for extensive stretches of time by interfacial powers.<sup>[10]</sup> A few stages were engaged with this peculiarity during bond development.<sup>[11]</sup> The peculiarities of polymer adherence to mucosal surfaces were not obviously portrayed, and five speculations for buccal adhesion were proposed.<sup>[12]</sup> Adsorption, dissemination, wetting, crack, and electronic hypotheses are all shared by all.

### BUCCALADHESIVE POLYMERS

Compared to conventional medication delivery techniques, bioadhesive formulations provide a number of benefits. They have the ability to extend the duration of drug residence at the application site, leading to a more consistent and regulated release of the medication. Additionally, they can minimize the dose frequency, which enhance patient compliance and decreases the possibility of unwanted effects. Choosing the right polymer is essential for creating bioadhesive formulations that work. The polymer must be non-toxic, biocompatible, and able to create strong connections with biological surfaces. Polymers including chitosan, hyaluronic acid, and polycarbophil are frequently utilized in bioadhesive formulations.

Bioadhesive details can be utilized in various applications, like medication conveyance, wound recuperating, also, tissue designing. For instance, bioadhesive patches can be utilized to convey drugs through the skin or mucosal layers, while bioadhesive gels can be utilized to elevate wound mending or to cover careful inserts to forestall contamination.

Overall, bioadhesive formulation can possibly upset drug conveyance and other biomedical applications by giving more compelling, designated, and enduring medicines. The utilization of bioadhesive details has become progressively famous in drug conveyance and tissue designing applications, as they can help to work on the viability and bioavailability of medications, and can give

a framework to tissue recovery.<sup>[13]</sup> Bioadhesive polymers are intended to stick to organic tissues, like mucosal films, and convey drugs or other restorative specialists.

The following physicochemical parameters that make a polymer bioadhesive which include

**Hydrophilicity:** Bioadhesive polymers should be hydrophilic, or water-cherishing, to communicate with the wet surfaces of organic tissues. This assists with advancing bond and further develop the contact season of the medication or restorative specialist with the tissue.

**Hydrogen bond-forming groups:** Numerous bioadhesive polymers contain practical gatherings that can shape hydrogen bonds with the mucin glycoproteins in bodily fluid, or with other biomolecules on the outer layer of the tissue. This assists with fortifying the attachment and drag out the home season of the medication or restorative specialist.

**Flexibility:** Bioadhesive polymers should be adaptable and ready to interpenetrate with the bodily fluid or epithelial tissue to frame areas of strength for a. This can assist with expanding the surface area of contact between the polymer what's more, the tissue, prompting better grip.

**Visco-elastic properties:** Bioadhesive polymers ought to have visco-versatile properties, and that implies they can twist under pressure and recuperate their shape when the pressure is taken out. This can assist the polymer with adjusting to the unpredictable surface of the tissue and keep in touch for a more drawn out timeframe.<sup>[14]</sup>

Adhesive polymers can be broadly categorized as charged or uncharged, natural or manufactured, and soluble or insoluble in water. To increase the amount of time that a medication is in touch with the buccal mucosa and improve buccal drug absorption, a variety of polymers were studied as buccal adhesives.

Delivery of drug through the oral cavity membrane may be classified as following<sup>[5]</sup>

- Sublingual medication Drug delivery framework conveyed the medication through mucosal film covering the floor of mouth into blood course.
- Buccal medication conveyance framework conveyed the medication through mucosal layer into blood circulation
- By placing an in the middle among cheeks and gums. Nearby medication conveyance framework conveyed the medication into the oral hole.

### MEASUREMENT OF BUCCALADHESIVE STRENGTH

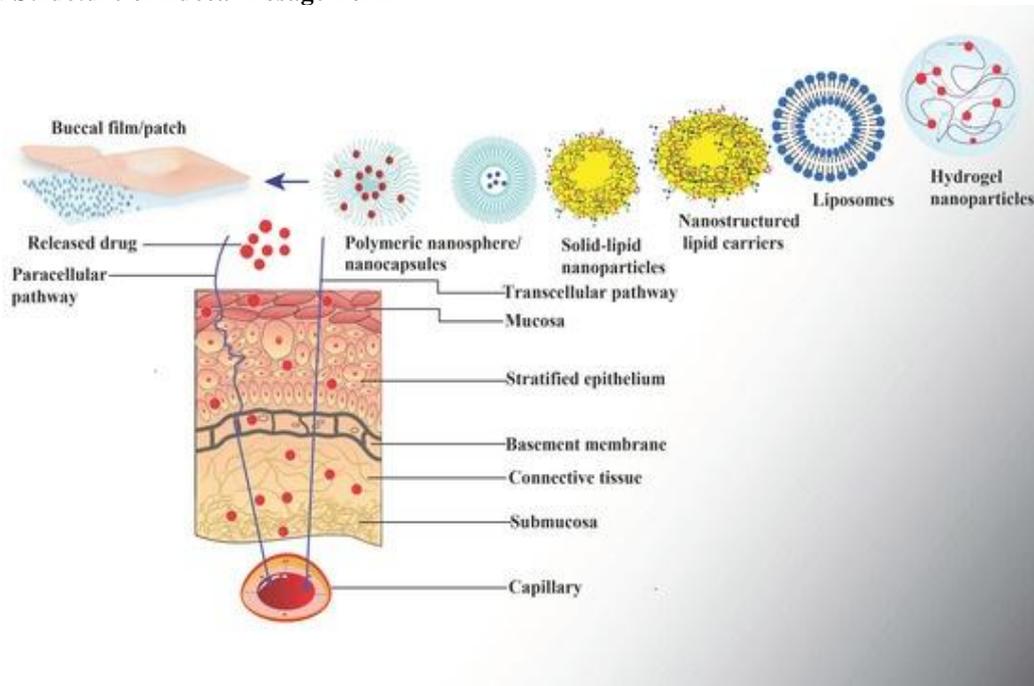
Different tests were performed to guarantee similarity, physical and mechanical dependability, surface examination, furthermore, bioadhesive bond strength, including enlarging, thickness, temperature impact on consistency, shear pressure strength, buccal glue

strength, falling circle technique, and segregating force estimation. These will give data about the polymers utilized in the definition.

**Contact Phase:** A close contact (wetting) happens with the mucoadhesive and bodily fluid layer together from a fair wetting of the bioadhesive and a film or from the expanding of bioadhesive.

**Consolidation Phase:** Different physicochemical collaborations, for example, hydrogen holding, hydrophobic cooperations and scattering powers, happens to solidify and give a lift to the cement joint, prompting delayed bond.<sup>[6]</sup>

**Design and Structure of Buccal Dosage Form**



**A. Matrix type:** The buccal patch's matrix structure combines a medication, an adhesive, and other components.

**B. Reservoir type:** In a repository framework the plan of buccal fix incorporate a cavity for a medication and parts

separate from the glue. To forestall the deficiency of medication, to lessen misshapening of fix and deterioration while in the mouth; and to control the heading of medication conveyance an impermeable sponsorship is applied.

**Buccal Bioadhesive Dosage Forms<sup>[9,10]</sup>**



**Buccal Bioadhesive Tablets:** Buccal bioadhesive tablets are dry measurements shapes that should be saturated

prior to being applied to the buccal mucosa. Bioadhesive polymers and added substances are now used to make

twofold and multifaceted tablets. These tablets are strong dose structures shaped by direct pressure of powder that can be put in touch with the oral mucosa and permitted to break down or stick contingent upon the sort of added substances remembered for the measurement structure. This measurements structure can convey medications to the mucosal surface or the oral depression in various bearings.

**Buccal Bioadhesive Semisolid Dosage Forms:** This dose structures contain regular or engineered polymers in powdered structure which is scattered in a polyethylene or in fluid arrangement.

**Buccal Bioadhesive Films and Patches:** This Type of patches incorporate multifaceted dainty film or two poly overlays that are oval or round in shape, containing of essentially of bioadhesive polymeric layer and impermeable sponsorship layer to permit unidirectional progression of medication across buccal mucosa. These movies are ready by consolidating the medicament in liquor arrangement of bioadhesive polymers.

**Buccal Bioadhesive Powder Dosage Forms:** This measurement structures are a combination of the medication and bioadhesive polymers and are showered onto the buccal mucosa the decrease in diastolic pulse after the organization of buccal film and buccal tablet.

#### Advantages of buccal drug delivery system<sup>[11]</sup>

- Drug is easily directed and annihilation of treatment in crisis might be worked with.
- Drug discharge for delayed span of time.
- In oblivious and injury patient's medication can be managed.
- Drug has high bioavailability since it sidestep first pass digestion.
- A few medications are unsteady in acidic climate of stomach can be regulated by buccal conveyance.
- Drug assimilation happens by detached dispersion.
- Because of close contact with the engrossing film surface, pace of retention is high.
- Quick beginning of activity.

#### Limitations of buccoadhesive drug delivery<sup>[12]</sup>

- Drugs which are unsteady at buccal pH can't be regulated.
- Drug having upsetting and harsh taste or a disgusting scent or causes bothering can't be given by this route
- Drug having little amount or portion must be given by this course.
- Drugs which are expected to be consumed by uninvolved dispersion just can be given by this course.
- Drinking and eating might be kept away from.

#### Factors affecting mucoadhesion<sup>[13]</sup>

- Polymer related factors: A few properties or qualities of the dynamic polymer assume a crucial part in mucoadhesion. Among them, focus, enlarging, polymer atomic weight, specific affirmation what's more, polymer chains adaptability that might influence the mucoadhesion.
- Climate related factors: pH of the polymer-substrate interface, useful strength and first contact time can impact the mucoadhesion.
- Physiological elements: Sickness state and mucin turn over are the significant physiological variables, which can likewise influence mucoadhesion.

#### Basic components of buccal drug delivery system are

**A. DRUG SUBSTANCE:** Prior to creating mucoadhesive medication conveyance frameworks, it is important to decide if the expected activity is for nearby or fundamental impact, as well concerning quick or delayed discharge. Pharmacokinetic properties are basic in the determination of fitting medications for the plan of buccoadhesive medication conveyance systems. The medication ought to have following qualities.<sup>[14]</sup>

- The ordinary single portion of the medication ought to be extremely less.
- The medications having natural half-life between 2-8 hrs are appropriate possibility for controlled drug delivery.
- Tmax of the medication shows many changes or higher qualities when controlled orally.
- Through oral course medication might show first pass impact or presystemic drug disposal.
- At the point when directed orally the medication ingestion ought to be inactive.

#### B. BIOADHESIVE POLYMER

The portrayal and choice of reasonable bioadhesive polymers in the plan is the most important phase in the definition of buccoadhesive measurement structures. Bioadhesive polymers are vital in buccoadhesive medication conveyance frameworks. Polymers are likewise utilized in grid gadgets, which encase the medication in a polymer framework and control the span of medication discharge.<sup>[15]</sup> Bioadhesive polymers are the most assorted class of polymers, and they have a great many applications in persistent medical services and therapy. The medication enters the mucous film by means of the center layer or rate controlling layer. Bioadhesive polymers that stick to the epithelial or mucin surface are successful and further develop the oral medication conveyance framework fundamentally.<sup>[16]</sup>

#### C. PERMEATION ENHANCERS

Penetration enhancers are agent that permit saturation through the buccal mucosa. The decision of pervasion enhancer and its not entirely settled by the medication's physicochemical properties, the idea of the vehicle, the site of organization, and different added substances.<sup>[18]</sup>

## EVALUATION OF BUCCAL DRUG DELIVERY SYSTEMS

### Physical evaluation

It comprises of three parts: content consistency, weight consistency, and thickness consistency. Weight variety was surveyed by looking at the typical load of ten haphazardly chosen patches from each group to the weight of a singular fix. The thickness of the film ought to be estimated in five places (the middle and four corners) and the mean thickness determined. Tests with scratches or tears, air bubbles, or a mean thickness variety of over 5% are barred from examination. Three patches having measurements 20 mm of every definition were taken independently in 100 ml volumetric jars, 100 ml phosphate cushion arrangement having pH 6.8 were added and blended constantly for 24 hours. The arrangements were sifted, weakened reasonably and break down by utilizing UV spectrophotometer. The normal of three patches was taken as conclusive perusing.<sup>[20]</sup>

### Drug-excipients interaction studies

Drug-excipient communication studies are significant during the definition and improvement of strong dose forms. To assess potential medication excipient collaboration concentrates on Differential filtering calorimeters (DSCs), X-beam diffraction (XRDs), Fourier Change Infrared Range (FTIRs), and dainty layer chromatography are all options. Differential filtering calorimeters are utilized for speedy assessment of potential inconsistencies in light of the fact that they show shifts in softening endotherms and exotherms, changes by all accounts, and varieties in the comparing response enthalpies.<sup>[19]</sup>

### Surface pH

The surface pH of the buccal not entirely set in stone to explore the chance of any in-vivo side effects. Since an essential or acidic pH can disturb the buccal mucosa, keeping the surface pH as close is basic to nonpartisan as could really be expected.<sup>[21]</sup> A consolidated glass cathode was utilized for this reason. The buccal patches were kept in touch with 1 ml of refined water (pH  $6.5 \pm 0.05$ ) and permitted to grow for two hours at room temperature also, pH was noted somewhere around acquiring the cathode contact with the outer layer of the fix and permitting it to equilibrate for 1 moment.<sup>[22]</sup>

### Swelling increases the weight of patch

A medication stacked fix of 1x1 cm<sup>2</sup> was kept and burdened a pre weighed cover slip, and afterward 50 ml of phosphate support (pH 6.6) was added. The cover slip was taken out after at regular intervals and weighed upto 30 minutes. The distinction in the loads gives the weight increment because of retention of water and enlarging of fix.<sup>[23]</sup>

### Ex vivo mucoadhesive strength

For deciding ex vivo mucoadhesive strength a changed equilibrium strategy is utilized. New buccal mucosa of

bunny or sheep acquired and utilized in no less than 2 hours of butcher. The mucosal film isolated by isolating fundamental fat and free tissues. The mucosal film were washed with refined water and afterward with phosphate cradle (pH 6.8) at 37 °C. The buccal mucosa cut into little pieces and again washed with phosphate support (pH 6.8). A piece of buccal mucosa was attached to the glass vial, which was loaded up with phosphate support. The two side of the changed equilibrium was made equivalent before the review, by putting a 5 g weight on the right-hand side of pan. A load of 5 g was eliminated from the right-hand side of skillet, which brought down the dish alongside the tablet over the mucosa. The equilibrium was saved for 5 minutes contact time here. Comparable to weight, the water was added at a sluggish rate with an imbue set of 100 drops each moment to the right-hand side of skillet until the tablet separated from the mucosal surface. This separation force gave the information on mucoadhesive strength of the buccal tablet in grams. The glass vial was firmly fitted into a glass measuring utensil loaded up with phosphate support (pH 6.8) at 37 °C  $\pm$  1 °C because of which it just touch the mucosal surface. The buccal tablet was adhered to the lowerside of a rubberstopper with cyanoacrylate cement.<sup>[26]</sup>

### Ex- vivo mucoadhesive time

The ex vivo mucoadhesion time performed after utilization of the buccal fix on newly cut buccal mucosa of sheep or hare. The new buccal mucosa was tied on the glass slide, and a mucoadhesive center side of every tablet was wetted with 1 drop of phosphate cushion (pH 6.8) and stuck to the sheep buccal mucosa by applying a light power with a fingertip for 30 seconds. The glass slide was then placed in the container, which was loaded up with 200 ml of the phosphate cushion having pH 6.8, and kept at 37 °C  $\pm$  1 °C. A 50 rpm blending rate was applied following two moment to reproduce the buccal hole climate, and tablet bond was observed for 12 hours. The time taken for the tablet to confine from the buccal mucosa was noted as the mucoadhesion time.<sup>[27]</sup>

### Drug release study (In vitro)

US Pharmacopeia (USP) XXIII pivoting paddle strategy used to concentrate on the medication discharge rate from the bilayered and diverse tablets. The disintegration medium comprise of phosphate support pH 6.8. The study was performed at 37 °C  $\pm$  0.5 °C, with a turn speed of 50 rpm. The support layer film of buccal tablet connected to the glass circle with moment cement (cyanoacrylate cement). The circle was appointed to the disintegration vessel's base. At foreordained stretches, 5 ml tests were taken out and supplanted with new medium. The examples were sifted through Whatman channel paper and broke down by UV spectrophotometry at fitting nm after suitable weakening.<sup>[28]</sup>

### Drug permeation study (In vitro)

Utilizing Keshary-Chien or Franz type glass dispersion cell, the in vitro buccal medication penetration

investigation of Drugs through the buccal mucosa of sheep or bunny is performed at  $37^{\circ}\text{C} \pm 0.2^{\circ}\text{C}$ . It incorporates the giver and receptor compartments in which a new buccal mucosa was tied. The center side of the buccal tablet was confronting the mucosa and the compartments clasped together. One ml phosphate cushion (pH 6.8) is put in benefactor compartment and phosphate cushion (pH 7.4) is put receptor compartment. The hydrodynamics condition was kept up with in receptor compartment by mixing with an attractive globule at 50 rpm. At a foreordained time period time one ml test can be removed and test for drug content at reasonable nm utilizing an UV spectrophotometer.<sup>[29]</sup>

### Mechanical Properties Measurement

The mechanical properties of the patches were assessed utilizing a chip based progressed force cloth and a mechanized test stand (West Sussex, Mecmesin, Ultra Test, Mecmesin, UK) with a 25kg burden cell. A film strip with aspects of 60 x 10 mm and no apparent imperfections was cut and situated between two braces isolated by 3 cm. Braces were intended to get the fix without smashing it during testing; the strips were pulled separated by the upper cinch moving at a pace of 2 mm/sec until the strip broke, while the lower clasp stayed fixed. The film's power and extension where the strip broke were recorded. The rigidity and extension at break values was determined utilizing the recipe.<sup>[31]</sup>

$$\text{Tensile strength (kg. mm}^{-2}\text{)} = \frac{\text{Force at break (kg)}}{\text{Initial cross sectional area of the sample (mm}^2\text{)}}$$

$$\text{Elongation at break (\% . mm}^{-2}\text{)} = \frac{\text{Increase in length (mm)}}{\text{Original length Cross sectional area (mm}^2\text{)} \times 100}$$

### Stability study in Human saliva

All clusters are exposed to a steadiness investigation of quick dissolving films as per ICH rules. The movies were assessed for crumbling time, drug content, and actual appearance after a foreordained time span. The strength investigation of advanced mucoadhesive fix detailing was performed at 40 C,  $37 \pm 5$  C and  $75 \pm 5$  % RH upto three months. Following three months, the upsides of all boundaries continued as before, with minor changes happening in the upsides of volume ensnarement efficiency, % lengthening, and % drug discharge later eight hours, which were huge.<sup>[30]</sup>

### Folding endurance

Collapsing perseverance of the not entirely set in stone by more than once collapsing one fix at a similar spot till it split or collapsed up to multiple times physically, which was viewed as agreeable to uncover great fix properties. The times the fix could be collapsed at similar spot without breaking gives the worth of the collapsing survival. This experiment is finished on five patches.<sup>[32]</sup>

### Viscosity

Fluid arrangements contains both polymer and plasticizer arranged in the very focus as that of the patches. A Brookfield viscometer model (LV DV-II) connected to a helipath shaft number four is utilized. The thickness estimated at room temperature at 20 rpm. The recorded qualities the mean of three conclusions.<sup>[33]</sup>

### Ageing

Bioadhesive patches were pressed in petri dish fixed with aluminum foil and set in a hatchery kept up with at  $37 \pm 0.5$  °C and  $75 \pm 5$  % RH for a considerable length of time. Changes in the delivery conduct, home time, appearance, and medication content of the put away fixes tried after 1, 2, 3, 4, 5 and a half year. The information

introduced the mean of three conclusions. New and matured cured patches, following a half year stockpiling, examined utilizing filtering electron magnifying lens.<sup>[34]</sup>

### CONCLUSION

Mucoadhesive buccal medication conveyance framework could be valuable for planning more up to date or novel mucoadhesive measurements structures. The article could give important data on the different mucoadhesive polymers, their attributes, and their expected applications in drug conveyance frameworks. Furthermore, the article might give experiences on the plan and assessment of mucoadhesive measurement structures, as well as the elements influencing their mucoadhesive properties and medication discharge energy. These snippets of data could be gainful for growing more viable and proficient mucoadhesive medication conveyance frameworks that could work on persistent consistence and remedial results. Mucoadhesive dose structure has application from different edges, with progression of novel mucoadhesives, format of the gadget, pervasion improvement and systems of mucoadhesion. With the presentation of a huge number of most recent medication particles in view of medicine disclosure, mucoadhesive drug conveyance will play a much continuously critical capability in conveying these particles.

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