Review Article

**Patented Pharmaceutical Reconstitutable Sustained Release Suspension**

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Reconstitutable suspension, Patents, Sustained Release (SR), Microencapsule, Drug delivey

**Abstract**
At the present time reconstitutable suspensions are obtainable in a market. Oral liquor suspensions are majorly designed for the patients with difficulty in swallowing. Reconstitutable suspensions necessitate water to prior for mixing. Sustained release (SR) suspensions aimed at controlling the rate of release by maintaining desire drug levels in the blood for long duration of time. An oral suspension could be the most excellent fitting dosage form intended for geriatric and pediatric patients. They comprise improvement of the rate and extent of drug absorption, higher patient compliance, reduction of side effects and taste masking of bitter drug. Reconstitutable SR suspensions are prepared by numerous novel approaches to design and development of variety of drugs. They are prepared by using a variety of polymer like Cellulose acetate, EC (Ethyl Celulose), HPMC phthalate, Eudragit, Xanthan gum etc. for enteric coating purpose, which are give controlled drug delivery from the granules. SR suspension developed into the research characterized by Scanning electron microscopy (SEM), particle size analysis, drug entrapment efficiency, and In-vitro Drug Release. SR suspension will be benefited to avoid fluctuations in blood drug plasma concentration and gives its action for an entire period of time.

**1. Introduction**
Oral drug delivery is the majority favored route of drug delivery. Suspensions are uniform dispersion of solid drug particles in a vehicle in which the drug has minimum solubility. Liquid dosage form is more favored than solid because of the flexible dosage administration and easy to swallow. In controlled release (CR) form is more patient compliant with less significant side effects and improved bio-availability.

Suspension is a dispersion system consists of; particulate matter (dispersed phase) and continuous medium (dispersion medium) and in which the internal phase is dispersed uniformly consideration the external phase. Suspensions are the biphasic liquid dosage forms of medicament in which the finely divided solid particles ranging from 0.5 to 5.0 micron dispersed in a liquid or semisolid vehicle. Suspensions are generally in use orally or by parenteral’s route. They are also used for external applications. The particle sizes of disperse phase play an important role in suspensions. To avoid gritty feeling to the skin and to cover a greater area of the applications, the suspension containing the smaller size of particles this is intended for external use. Moreover the smaller particle can penetrate easily into the skin and gives the faster dissolution. For the parenteral’s suspension particles having the as much size that easily pass through needle. The particle size of dispersed phase should not above than 10 micron. Suspensions are commercial dry mixtures that require the addition of water at the time of dispensing so, there is requires mixing prior to administration. Formulated suspension is first choice when drug stability is a major concern\[1,2\].

**2. Formulated ingredients for reconstitutable SR suspension**
Selecting ingredients are based on both suitability for reconstitution and the physical type of powder mixture product. There are ingredients separated into two categories of frequent and infrequent use. Majority drug formulated as Reconstitutable oral suspensions mainly are antibiotics. Frequent used ingredients are suspending agents, wetting agents, sweetener, preservatives, flavors, colors and buffers etc. Infrequent used ingredients are anti-caking agents, flocculating agents, solid diluents, antifoaming agents, granule binders, granule disintegrants, antioxidants and lubricants.

<table>
<thead>
<tr>
<th>No</th>
<th>Ingredients</th>
<th>Examples</th>
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<tbody>
<tr>
<td>1</td>
<td>Suspending agent</td>
<td>Acacia, CMC sodium, Iota-carrageenam, MCC with CMC sodium, Povidone, Propylene glycol alginate, Silicone dioxide, Colloidial, SSG, Tragacanth and Xanthan gum</td>
</tr>
<tr>
<td>2</td>
<td>Wetting agent</td>
<td>Polysorbate-80, Acacia, Tragacanth, alginate, Gaur gum, Pectin, Gelatin, Wool fat, Egg yolk, Bentonite, Veegum and Methyl cellulose</td>
</tr>
<tr>
<td>3</td>
<td>Sweetener</td>
<td>Sucrose, Mannitol, Dextrose, Aspartame and Sodium saccharin</td>
</tr>
<tr>
<td>4</td>
<td>Preservative</td>
<td>Propylene-glycol, Benzalkonium chloride, Benzonic acid, Cotrimide, Cholorohexadene, Disodium EDTA etc.</td>
</tr>
<tr>
<td>5</td>
<td>Antioxidants</td>
<td>Ascorbic acid, Tocopherols, Butylated hydroxy anisole (BHA), Butylated hydroxytoluene (BHT), Sodium bi sulfite, Sodium sulfate acetone, thio glycerol, cystine, acetylcystine</td>
</tr>
<tr>
<td>6</td>
<td>Flavor</td>
<td>Raspberry, Pineapple and Bubble gum</td>
</tr>
<tr>
<td>7</td>
<td>Buffer</td>
<td>Citric acid is most preferable used to stabilize pH of suspension between 3.5-5.0%, acetates 1-2%, citrates 1-5%, and phosphates 0.8-2% etc.</td>
</tr>
<tr>
<td>8</td>
<td>Color</td>
<td>(i) White; Titanium dioxide, Blue-brilliant blue, indigo carmine, indigo, (ii) Red-amaranth, carmine, (iii) Yellow- taratartarazine, sunset yellow, carrots, annatto seeds, madder plant, (iv) Green-chlorophyll, (v) Brown- caramel etc.</td>
</tr>
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3. Qualities of ideal Suspension [3,5]

A well formulated suspension should have the following properties:
- The dispersed particle should not settle readily and the settle should re-dispersed immediately on shaking. The easy re-dispersion of sediment particles in a suspension is important for uniformity of dose.
- The particles should not form a cake on setting.
- The viscosity should be such that the preparation can be easily poured. A highly viscous suspension would make pouring difficult.
- It should be chemically and physically stable.
- It should be palatable (oral use).
- It should be free from gritting particles (external use).
- It should be chemically inert.
- The dispersed particles are small and uniform.
- It should be free from large particles which spoil its appearance, give a gritty taste to oral preparations and also cause irritation to sensitive tissues when applied externally.

4. Challenge in formulation of oral suspension

- Physical stability: The properties of a solid-liquid dispersion system alter the physical stability as well as the absorption rates of the formulation.
- An acceptable organoleptic property like taste is hard to achieve and thus reduce the patience compliance.

5. Method of Preparation [4,5,6]

a) Ion exchange resin (IER) technique
b) Saturated drug suspension as a suspending medium.
c) Using non aqueous vehicle.
d) Using reconstitution technique
e) By using protective coating method
f) Emulsion-solvent evaporation (o/w, w/o, w/o/w) methods
g) Polymerization by phase separation methods
h) Microencapsulation Methods

Two types of microencapsulation system include physical and chemical methods:
- Physical method
  - Air suspension coating
  - Rotary disk atomization
  - Fluidized bed coating
  - Stationary nozzle co-extrusion
  - Submerged nozzle co-extrusion
  - Centrifugal extrusion
  - Multi-orifice centrifugal process
  - Spray drying and congealing techniques
  - Pan coating
- Chemical method
  - Co-acervation phase separation
  - Solvent evaporation techniques
  - Polymerization
  - Liposome technology
  - Nano-encapsulation
  - Solvent extrusion
  - Simplex and complex co-acervation

6. Novel Pharmaceutical Reconstitutable suspension

Jaber SH et al. formulate the Azithromycin suspension as an oral dosage form was carried out to prepare an acceptable suspension either as dry physical mixture or granules to be reconstituted, through studying the effect of various type and concentration of suspending agent [xanthan gum, Hydroxy propyl methyl cellulose (HPMC), either alone or combination] on the release profile of drug [7].

Sabri AS et al. prepare a stable suspension for rifampicin through preparation of different formulas of rifampicin aqueous suspension either as ready to use or as granular powder to be reconstituted. The chosen formulas was evaluated and compared with marketable brand to rifampicin as a reference through measuring their dissolution rates and other physical properties of result indicate that the selected formula have better dissolution rate compared with the reference suspension and the rheogram showed that the selected formula was less viscous than the reference one. Also, it was establish that the granular rifampicin was more stable than the ready to use suspension, because the expiration date of granular rifampicin was 2.6 years, while the expiration date of ready to use suspension was 1.8 years [8].

Akre HS et al. prepare dry suspension of taste masked antibiotic drug intended for pediatric use. This is marketable dry mixtures that need addition of water at the time of dispensing. People require effective drugs that contain a nice taste so, can be administered easily. So, need to mask the unpalatable taste of a drug in order to improve the product quality. The solvent evaporation process is used for microencapsulation. Edragit L100 is used as taste masking agent. FT-IR study shows that there is no significant interaction occurring between drug and excipient [9].

Aejaz A et al. prepare ready use suspension of amoxicillin trihydrate used as antibacterial agent. It has poor stability in presence of water having shorter shelf life of about a week upon reconstitution. Therefore, it is try to formulate in to ready oral suspension with improved stability and shelf life. In the initial approach, water was used as suspending medium and pH of formulation was selected in the range of 5 to 6.5. Particle size determination revealed that majority of particle was in the size range of 15-75 mm [10].

Jain DK et al. prepare reconstitutable oral suspension of ambroxol HCl and azithromycin. Reconstitutable oral suspension show adequate chemical stability of the drug during shelf life, avoids the physical stability problems. These are dry mixtures that require the addition of water at the time of dosing. The reconstitutable oral suspension of azithromycin and ambroxol HCl were found to be stable over its intended shelf life of 15 days after reconstitution. Formulation with xantham gum (1.5% and 0.75%) showed excellent sedimentation volume and degree of flocculation nearing 1, and this was due to presence of anti caking agents or the granules disintegrate added to the formulations. Also formulation with acacia (3% and 1.5%) showed good redispersibility [11].

Kathpalia H et al. prepare ready use cefpodoxime proxetil suspension. Antibiotics are not chemically stable in water based on pharmaceutical suspensions. Anhydrous liquid antibiotic suspension for oral administration provides a product having good shelf life and taste characteristics relative to conventional liquid formulations. A ready to use oil based cefpodoxime proxetil preparation which can be stored at room temperature was prepared and evaluate. The formulation showed improved redispersibility, good taste masking of the bitter drug and allows the product to be stored longer preventing hydrolysis of the drug [12].

Prandaya PS et al. design and develop oral reconstitutable system of cephalosporin as dry syrup to be reconstituted with water and then given to children. It was also aimed at determining the influence of different processing conditions like powder mixture, granulation and compilation product on the properties of the drug product. All the formulations showed good organoleptic properties with enhanced sedimentation and rheological behavior with t_{95} within two hours. The powder mixture gave a rapid release of 10-30 minutes [13].
Vinod et al formulate taste masked cefuroxime axetil dry suspension. The bitter tastes of cefuroxime axetil greatly hamper the further development of suitable formulations of this drug for oral use and it is important to mask the bitter taste and also make them better for oral use. Lubritab is used as a taste masking agent. The taste masked dry suspension was made by compaction process. The prepared suspension was evaluated for various parameters like sedimentation volume, degree of flocculation, drug content and in-vitro dissolution profile and found to be within limits[14].

Sateesha et al prepare formulation and stability study of palatable norfloxacin dry syrup: comparison amongst different preparation methods. Hence an attempt is finished to develop norfloxacin dry syrup. Methods working for formulation are: (i) preparation of norfloxacin granules by coating with different levels of acrycoat E100-40 and (ii) preparation of norfloxacin microspheres using Eudragit E100 and subsequent adsorption on different carrier such as lactose, MCC and mannitol. The microspheres were smoother and more regular in their shape compared to the granules [15].

Williamson et al prepare improving suspendibility of a water-insoluble active in a reconstitutable powder for oral suspension. The suspendibility of a water-insoluble drug are improved on a sorbitol based reconstitutable powder for oral suspension using two novel excipient sentry™, polyox™ WSR N80, NF (polyethylene oxide) and avicel CL-611®/NF (MCC /CMC sodium) [16].

7. Patents on Reconstitutable suspension

Van LA and his collaborator (1994) formulate aqueous pharmaceutical suspension with process intended for preparation thereof. The present invention relate toward an aqueous pharmaceutical suspension contain suspended acetaminophen and at least one added pharmaceutical active, a suspension method contain xanthan gum, a combination of MCC and sodium CMC and an ancillary suspending agent chosen from the group consisting of hydroxyethyl cellulose and a pharmaceutically suitable salt of CMC, an useful quantity of a taste-masking composition; and water, as well as a procedure for producing such aqueous pharmaceutical suspensions [17].

Romanperez S and his coworker (1996) developed an aqueous or T-butanol solvent methods, superficial reconstitute, and submicron-reconstitute preliposome-lyophilate and process of its preparation and use. In one byword, a modified technique designed for the preparation of a submicron and firm liposome formulation of the non cross-resistant anthracyclineanycamicin is preferred[18].

Mannalalram GB and his coworker (2005) developed the present inventions discloses a novel drug delivery system for proton pump inhibitors comprising benzimidazole compounds or their salts, preferably rabeprazole or its salts and pharmaceutically suitable excipients in powder form which is reconstitutable in a parenterally adequate solvent to form an injectable solution[19].

Gerald LM and his coworker (2007) developed the present creation provide aqueous oral formulations contain sertraline or a pharmaceutically suitable salt thereof in addition to sufoalkyl ether cyclodextrine. The liquid formulation can be administered directly or diluted before administration[20].

Guimberteau and his coworker (2007) prepare the anti-misuse micro-particle oral pharmaceutical dosage form. The invention relate to a solid oral pharmaceutical form which is characterise into that it contain anti-misuse means, in that at least part of the active principle it comprise is limited in coated microparticles for modified release of the active principle, and in that the coated microparticles include a coating layer which assure modified release of the active principle and simultaneously impart crashing resistance to the coated microparticles so as to avoid abuse[21].

Santiago DC and his collaborator (2008) developed an immunosuppressive macrolide powder designed for oral suspension. The present invention describe pharmaceutical compositions so as to comprise a Tacrolimus powder designed for oral suspension that exhibits immense stability as a powder for suspension and also, formerly prepared as the extemporaneous suspension, lacking the formation of cake similar to clusters, same having a acceptable flavor and a satisfying smell. The invention also describes the method for preparing the pharmaceutical compositions, same create a dry process that contain mixing Tacrolimus and pre-sieved pharmaceutically suitable carriers for a appropriate length of time and the use of the pharmaceutical compositions for treat and prevent rejection of transplanted organs and atopic dermatitis[22].

Frans W and his coworker (2008) formulate the heat stable flavouring compositions. One aspect of the present invention relates to particulate flavouring compositions having, based on the total weight of the composition, 0.1-40 wt % of flavouring substances, 10-90 wt % of one or more hydrocolloids, and 0.1-50 wt % of a lipid material having a melting point above 75° C. These flavouring compositions are mainly suitable for application in food products (including beverages), the preparation of which involves one or more heat processing steps, as well as in confectionery products such as chewing gum. Other aspects of the invention relate to a method of producing a particulate flavouring work of art, to a food product containing such a flavouring composition and to a process of developed a reconstitutable food product [23].

Mitsuho S and his coworker (2008) develop the solid milk and method for manufacturing thereof. The object of the present invention is to provide solid milk having suitable solubility and strength and a method for manufacturing such solid milk. The present invention is based on the knowledge that solid milk combining sufficient strength with sufficient solubility can be obtained basically by compacting and molding only powdered milk as an ingredient under a condition where porosity and free fat content thereof are controlled within fixed ranges and then humidifying and drying. The above-described object can be attained with solid milk with a porosity of 30% to 50% and a method for manufacturing solid milk, comprising a compacting process for compacting powdered milk and obtaining a solid compacted body of powdered milk, a humidifying process for wetting the compacted body of powdered milk obtained in the compacting process, and a drying process for drying the compacted body of powdered milk humidified in the humidification process [24].

Jeffrey B his coworker (2008) formulate the Pharmaceutical Composition, A novel pharmaceutical composition comprising the NK3 receptor antagonist talnetant, povidone, mannitol and a surfactant, and a process for its preparation are disclosed[25].

Matthias R his coworker (2008) formulate the sterile suspensions of slightly soluble basic peptide complexes and pharmaceutical formulations containing them, the invention provides sterile suspensions and sterile lyophilizes of slightly soluble basic peptide complexes, and pharmaceutical formulations comprising them. The provided sterile suspensions, sterile lyophilizes and pharmaceutical formulations comprising them are particularly suitable for use in a parenteral dosage forms as medicaments for the treatment and prophylaxis of diseases and pathological states in mammals, especially in humans[26].

Travis M and his coworker (2008) prepare the prodrugs of phentermine. The invention relates to compositions of amino acid and peptide conjugates comprising phentermine. Phentermine is covalently attached to at least one amino acid via its amine group to the N-terminus, the C-terminus, and a side chain of the peptide carrier. Also discussed are methods for treating obesity[27].
Stephane G his coworker (2009) formulate the gas-filled micro-vesicles with polymer-modified lipids, Image enhancing contrast agents for use in diagnostic and/or therapeutic methods, particularly in the form of gas-filled micro-vesicles, with enhanced stability. The gas-filled micro-vesicles are stabilized by a layer of amphiphilic material and comprise from 0.15% to 1.0% by moles of a lipid bearing a hydrophilic polymer. The lipid bearing a hydrophilic polymer is preferably a phospholipid linked to polyethyleneglycol [28].

Stephen HW and his collaborator (2009) prepare the use of magnesium stearate dihydrate for lubrication of solid pharmaceutical compositions. The lubricant compositions may be used to lubricate a variety of bioactive formulations including pharmaceutical compositions [29].

Randal JK and his coworker (2010) prepare the Selective targeting of intra-tumoral cells, the present creation relates to the field of tumor growth and biology synergistic effects of combined administration of mirtazapine and a stimulant compound, the discovery discloses combination therapies and formulations of a stimulant (e.g., amphetamine) and mirtazapine and their methods of use [30].

Rajeev G his co-worker (2010) formulates the stable nanoparticulate drug suspension. A liquid pharmaceutical composition comprise an aqueous medium having suspended therein a solid particulate Bcl-2 relatives protein inhibitory compound for example ABT-263, having a D90 particle size not greater than about 3μm; wherein the aqueous medium further comprises at least one pharmaceutically acceptable surfactant and at least one pharmaceutically acceptable bisingivating agent such as sodium bicarbonate in amounts that are effective together to inhibit particle size increase. The composition is suitable for oral or parenteral administration to a subject in need thereof for treatment of a disease characterized by over expression of one or more anti-apoptotic Bcl-2 family proteins, for example cancer [31].

Brian A Salvatore and his coworker (2010) formulate the liposomal formulations of tocopherol amides. Formulate N-chromanol dicarboxylic acid derivatives and their bioisosteres in liposomal systems. Lyophilized liposomal dosage forms of N-chromans, are found to be stable, to achieve therapeutically meaningful plasma levels on administration to a mammalian host, and to demonstrate selective pro-apoptotic oncolytic properties in vivo. Advantageously, these formulations overcome the systemic toxicity that characterized their administration by other dosage forms [32].

Jerry TT his collaborator (2010) formulates the formulations for treating human and animal diseases. The present disclosure provides for a scientific formulation helpful in the management and anticipation of human and animal disease. A biologically effective amount of each of the components of the formulation is administered to patients in pill (or capsule) form via multiple different and identifiable pills. The compounds of the formulation are segregated into different pill types, and contain various amounts of the compounds curcumin, genistein, squalamine, vitamin E, N-acetyl-cysteine, methyl selenocysteine, zinc gluconate, B complex, lentinatin, Coenzyme Q10, Acetyl-L-carnitine, Lipidic acid, resveratrol, and vitamin C. Furthermore, Arabinoxylan and/or Peperine might be added to the various pill formulations [33].

Travis CM and his coworker (2010) prepare the polar hydrophilic prodrugs of amphetamine and additional stimulants and processes designed for making and using the same. Disclosed are polar, hydrophilic stimulant prodrug compositions comprising at least one stimulant chemically attached to a polar hydrophilic ligand, a salt thereof, a derivative thereof, or a combination thereof [34].

Vincent A his coworker (2010) formulates the sulfaalkyl ether cyclodextrin compositions, SAE-CD compositions are provided, along with methods of making and using the same. The SAE-CD compositions comprise a sulfaalkyl ether cyclodextrin having absorption of less than 0.5 A.U. due to a drug-degrading agent [35].

Catherin C and his coworker (2011) developed the inventions relates to the pharmaceutical formulations for oral administration with the modified release of active principle, excluding amoxicillin, said formulation consisting of suspensions of a coated particles of active principle. According to the invention, the microcapsule constituting the disperse phase of the suspension are designed to allow the modified release of active principle, according to a profile that does not change during the storage of the liquid suspension to do this the inventors propose the selection of a specific coating composition for the microcapsule which consist at least four components that allow these microcapsules to be stored in water without modifying their properties of modified release of the active principle, this liquid phase furthermore being saturated with active principle [36].

James DP his coworker (2011) formulates the inhalant formulation containing sulfaalkyl ether cyclodextrin and corticosteroid prepared beginning a unit dose suspension, an inhalable unit dose liquid formulation containing SAE-CD and corticosteroid is provided. The formulation is adapted for administration to a subject by nebulization with any known nebulizer. SAE-CD present in the formulation significantly enhances the chemical stability of corticosteroid, such as budesonide. The formulation can also be administered by conventional nasal delivery apparatus. The formulation is prepared by mixing SAE-CD, in solid or liquid (dissolved) form, with an inhalable suspension-based unit dose formulation [37].

Hans B his coworker (2011) formulates the pH-dependent controlled release pharmaceutical composition designed for non-opioids as a result of resistance by the influence of ethanol. The creation relates to a pH-dependent controlled release pharmaceutical composition, comprise on least one pharmaceutical active ingredient, with the exception of opioids, wherein the core is coated at least by one coating layer, controlling the release of the pharmaceutical composition, wherein the coating layer comprises a polymer mixture of (i) 40-95% by weight, based on dry weight of the polymer mixture, of at least one water insoluble essentially neutral vinyl polymer or copolymer, and (ii) 5-60% by weight, based on dry weight of the polymer mixture, of at least one anionic polymer or copolymer, which is insoluble in a buffered medium below pH 4.0 and soluble at least in the range from pH 7.0 to pH 8.0, characterized in that the coating layer further comprises 110 to 250% by weight of a non-porous inert lubricant, 1 to 35% by weight of at least one neutral cellulosic compound and 1 to 25% by weight of at least one emulsifier, each calculated on dry weight of the polymer mixture [38].

Ravis M his coworker (2011) prepare the antidepressant prodrugs, the creation provides antidepressant prodrugs comprising an antidepressant conjugated to one or more amino acids. The creation also relates to pharmaceutical compositions comprising an antidepressant prodrug, and toward methods of preparing and using the same [39].

Kavash M his collaborator (2011) prepares the discerning targeting of intra-tumoral cells, the present creation relates to the field of tumor enlargement and biology. The creation relates to behavior and characters of tumor-associated macrophages, and uses of such designed for the diagnosis and treatment of cancer and tumor growth [40].

John M and his co-worker (2012) developed a controlled release oral pharmaceutical dosage forms comprising MGBG. Disclosed herein do controlled release oral pharmaceutical dosage forms comprise MGBG, in addition toward their use for the enhanced management of illness with reduced side effects and longer time on greatest concentrate of them [41].

Ketan M and his co-worker (2012) developed an orally effective methylphenidate extended release powder and aqueous suspension product. An oral methylphenidate powder which is
reconstitutable into a final oral aqueous sustained release formulation containing at least about 50% or at least about 80% by weight base on the total weight of the suspension is provided. The powder is a blend containing a combination of an uncoated methylphenidate – ion exchange resin complex, a barrier coated methylphenidate – ion exchange resin complex-matrix and a water soluble buffering agent such that, upon formed into an aqueous liquid formulation. Following administration of a single dose of the oral methylphenidate suspension, a therapeutically effective amount of methylphenidate is reached in less than one hour and the composition provides a twelve-hour extended release profile [42].

Ulrich J and his collaborator (2012) the discovery relate toward tapentadol (i) used for the treatment of pain in a subject suffering from depression and or from anxiety and or (ii) used for the treatment or the prevention of depression and or of anxiety [43]. Ketan M and his coworker (2012) formulate the abuse resistant opioid drug-ion exchange resin complexes having hybrid coatings. A continuous release formulation used for opioid drugs is described. The formulations contain an opioid-ion exchange resin complex have a hybrid coating. The hybrid coatings contain a cured polyvinylacetate polymer and a pH-dependent enteric coating layer assorted therein. Also provided are methods of production and using same [44].

Sarjit J and his colleague (2012) formulates the method for drying biomaterials. The present invention provides a means to concentrate, dry and formulate biomaterials such as polysaccharides, gums and linked biopolymers, and microorganisms such as cells, spores, and the like from dilute solutions using spent germ and added oil bearing residues. In adding, the exhausted germ can serve up as a carrier for such biomaterials. The sorbed materials are useful in animal feeds [45].

Joseph AR and his coworker (2012) formulate the careful targeting of intra-tumoral cells, the present invention relates to the meadow of tumor growth and biology methods of treating cancer, Described are methods and compositions designed for treating epithelial tumors through a folate-vinca conjugate in combination with at least one other chemotherapeutic agent in which the tumors include ovarian, endometrial or non-small cell lung cancer tumors, as well as platinum-resistant ovarian tumors and platinum-sensitive ovarian tumors [46]. Daniela S his coworker (2012) formulates the method for treating chronic pain; the present invention provides anagaseic compounds comprise on at least one customized metalloporphyrin compound. Furthermore provide are methods to treat pain in orally administer an anagaseic compounds comprising at least one modified metalloporphyrin compound [47].

John MF and his collaborator (2012) prepare the whole seed processing and controlled viscosity crop, a method provide a pulverized entire seed product from a whole seed have 0.01% by total weight of oil therein. The whole seed is added to an aqueous carrier which physically milled at a shear rate of at least 3000 RPM. The shearing is continued until at least 50% by weight of seed solids will pass through a square mesh screen having 1.2 mm screen whole dimensions. The solids in aqueous carrier are collected as a suspension or dispersion in the aqueous carrier. The collected seed solids in aqueous carrier are dried to form a free-flowing powder. The free-flowing powder is rehydrated with a second aqueous medium to form a non-mucilaginous suspension or dispersion [48].

Leona GF his partner (2012) prepare the cosmetic sampler sheet, a cosmetic sample sheet is provided which includes cosmetics enclosed inside or under a solid, water-soluble polymeric film, and supported by a substrate sheet. The cosmetics are easily reconstitutable by a consumer to permit the consumer to seek different shades or colors of particular cosmetics [49].

Paul RR his coworker (2012) formulate the nutritionally enhanced part from rice bran and process of lowering insulin resistance using same, nutritionally enhanced nutraceutical hydrophilic and lipophilic rice bran fractions as of rice bran are provided, as well as a method of using the same to reduce insulin resistance in animals, especially humans with pre-diabetes and type-2 diabetes or others with symptoms of metabolic syndrome. Steps are provided with evaluating insulin resistance parameters, initiating therapy as well as providing therapeutic amounts of hydrophilic and lipophilic rice bran fractions from rice bran to treat pre-diabetes and type-2 diabetes or others with symptoms of metabolic syndrome, managing compliance with the therapy, and monitoring and reevaluating the therapy [50].

Walker AL and his associate (2012) formulate the injectable meclizine formulations and methods. Methods of treating a vertigo, nausea, or vomiting condition comprising injecting a subject with a pharmaceutically suitable formulation consisting fundamentally of an effectual amount of meclizine or a pharmaceutically acceptable salt thereof, a chemically adapted cyclodextrin, and an aqueous carrier medium having a pH among concerning 2 and about 7 are disclosed [51].

Harshal AJ and his associate (2013) developed a stable, taste masked, ready to use suspension comprising rifaximin dispersed in a suspension base and one or more pharmaceutically acceptable additives. Also provide is a procedure for preparing a stable, taste masked, ready to employ suspension of rifaximin comprising the steps of mixing, Rifaximin with the suspension base and further sizing the particles of rifaximin by way of milling the suspension to get homogenously dispersed rifaximin suspension [52].

Balasingam RK and his colleague (2013) developed pharmaceutical compositions and uses thereof the invention features pharmaceutical composition including (i) a drug (ii) a PEG fatty acid ester or PPG fatty acid ester in an amount satisfactory to increase the oral bioavailability of the drug [53].

Alexander VK his collaborator (2013) formulates the water soluble fullerene formulations and way of use thereof. The present inventions provide water soluble fullerene formulations and methods of use thereof [54].

Ramon P and his helper (2013) formulate the make use of pten-long head sequence for transmembrane deliverance of molecules. A composition for delivering cargo molecules across biological membranes is provided comprising (i) a peptide comprise following amino acid residue have the series put onward in “SEQ ID NO 1” for the move of a cargo molecule across a biological membrane and (ii) the cargo molecule, wherein the cargo molecule is not a peptide comprising amino acid residue have the series set onward in “SEQ ID NO 4”. Methods of delivering cargo molecules across biological membranes are also provided. Methods of treating a tumor, cancer, a metabolic disorder, and a cardiovascular disorder are also provided [55].

Arman S and his coworker (2013) formulate the method and composition to improve mechanical resistance of teeth, provide are composition and method for preventing dental caries, as well as aqueous composition and method for improving the mechanical strength of teeth [56].

Chi TH and his coworker (2014) prepare the “Hydroxylated Polymethoxy Flavone” compositions, provide herein are composition enriched in “Polyhydroxylated Polymethoxy Flavones” valuable as dietary supplement, food additives, pharmaceutical and nutraceutical and cosmetic composition [57].

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8. Characterization of Suspension [3, 5]

8.1 SEM analysis

Scanning electron microscopy (Joel JSM -840A, Japan) / (JSM-5410LV, Joel, Tokyo, Japan) was used to examine the shape and surface morphology of the ethyl cellulose microcapsules. Samples of microcapsules were dusted onto double-sided tape on an aluminum stub. The stubs were then coated with gold using a cold sputter coater to a thickness of 400 Å. The samples were imaged using a 25KV electron beam.

8.2 Microscopy studies

The microscopic observation of suspended microparticles was determined using an optical microscope.

8.3 Repose angle

For measuring a repose angle of suspension powder, it was passed through a conical flask which had a 0.9 cm diameter and was laced 10 cm above the horizontal surface. The height (h) of the heap formed was measured with a cathometer and the radius (r) of the cone base was also determined. Angle of repose (Φ) was calculated from following equation: Φ=tan⁻¹(h/r)
8.4 Rheology

The Rheology of the suspension was characterized using a Brookfield viscometer (meter RM180) with measuring bob no.2 and measuring tube no.2.

8.5 Sedimentation volume:

The sedimentation volume (F) was obtained based on the following equation: \( f = \frac{v_1}{v_0} \) in which, \( v_1 \) is the equilibrium volume of sediment and \( v_0 \) is the total volume of suspension. For equilibrium volume of sediment the sediment volume which remains unchanged for 3 weeks was considered.

8.6 Degree of flocculation

Degree of flocculation (\( \beta \)) was estimated by the following equation: \( \beta = \frac{f}{f_0} \) in which, \( f \) is the sedimentation volume of the flocculated suspension and \( f_0 \) is the sedimentation volume of the suspension when deflocculated.

8.7 Ease of redispersibility

For determination of ease of redispersibility (N), the number of shears required for redispersibility of a cylindrical glass graduate containing dispersed suspension, was considered.

8.8 Freeze/thaw cycles

Inspection of physical and microscopic changes of suspension undergoing sudden thermal changes was conducted. During this test suspensions were kept in a 40°C oven for 24 h and then transferred to a 0°C freezer for 24 h.

8.9 Normal temperature fluctuation

Inspection of physical and microscopic changes of the suspension which occurred during a gradual decrease in temperature from 40°C to -5°C was also performed. For this purpose, suspensions were kept 24 h in each temperature.

9.10 pH of suspensions

pH of suspensions was determined using a rot ring pH meter.

9.11 Drug release studies:

Drug release studies by using the USP paddle method according to the official method and condition.

9.12 Kinetic models

The goodness of fit of release data was tested with the mathematical models as the following:

First-order kinetic: \( \ln W = \ln W_0 - Kt \)

Squire-root of time: \( W = W_0 - Kt \)

Where \( W \) is the amount of drug remaining to be released and \( W_0 \) is the initial amount of drug.

9.13 Statistical analysis

Each formulation was prepared in duplicate, and each analysis was duplicated. Statistical analysis of the data was performed using analysis of variance (single factor) with the aid of Microsoft Excel. Differences were considered significant when \( P < 0.05 \).

9.14 Stability studies

The accelerated stability study was done in order to determine the expiration date of formulation by placing formulation or samples in oven at 40°C, 50°C and 60°C for 90 days. Samples (dry physical mixture powder or granules) were taken for their drug content at a suitable time intervals using UV spectrophotometric method for the accepted formulation and also, physical stability (color, odor and pH) changes for the samples were examined.

9. Marketed formulation of controlled release suspension

### Table 1: Marketed Formulations of controlled release suspension

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Zmax SR</td>
<td>Azithromycin Di-hydrate</td>
<td>Pfizer</td>
</tr>
<tr>
<td>2</td>
<td>Delsym</td>
<td>Dextromethorphan HBr</td>
<td>Reckitt Benckiser</td>
</tr>
<tr>
<td>3</td>
<td>Paxil</td>
<td>Paroxetin HCL</td>
<td>Gsk</td>
</tr>
<tr>
<td>4</td>
<td>Nexium</td>
<td>Esomeprazole</td>
<td>Astra Zeneca</td>
</tr>
<tr>
<td>5</td>
<td>Micro-k</td>
<td>Potassium chloride</td>
<td>THER- Rx Corp.</td>
</tr>
<tr>
<td>6</td>
<td>Tussionex</td>
<td>Hydrocodone and chlorpheniramine</td>
<td>Ucb</td>
</tr>
<tr>
<td>7</td>
<td>Dynabist-er</td>
<td>Chlorampheniramine and Pseudoephedrine</td>
<td>Wolters Kluwer Health</td>
</tr>
<tr>
<td>8</td>
<td>Augmentin®</td>
<td>Amoxicillin and Potassium clavunate</td>
<td>GlaxoSmithKline</td>
</tr>
</tbody>
</table>

10. Conclusion

Reconstitutable SR suspension is a method to increase the duration of drug action being formulated without affecting onset of action. SR suspension affected by coating the drug to be formulated as suspension by insoluble polymer coating. The polymer coating provides sustained release action and also masks the taste of the bitter drug. Among the oral reconstitutable controlled release suspensions are becoming more popular. Because they pass through the gut as if a pass through the gut as if a

Conflict of Interest

The author declares no conflict of interest.

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Reference


