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(54) Title: CHEWABLE PRODUCT INCLUDING ACTIVE INGREDIENT

(57) Abstract: Products and methods of delivering medicaments are provided. The product includes a consumable center and a compressible powder that is compressed around the center. The powder includes a medicament that may or may not be encapsulated.

SPECIFICATION

TITLE

"CHEWABLE PRODUCT INCLUDING ACTIVE INGREDIENT"

This patent application is a continuation-in-part of U.S. Patent Application Serial No. 09/681,935 filed on June 28, 2001.

BACKGROUND OF THE INVENTION

The present invention generally relates to the delivery of medicaments and agents. More specifically, the present invention relates to the delivery of medicaments and agents using chewable products.

It is of course known to provide agents to individuals for a variety of purposes. These agents can be used to treat diseases and as such are typically referred to as drugs or medicaments. Likewise, the drugs or medicaments can be used for prophylactic purposes. Still, it is known to provide agents to an individual for a variety of nonmedical purposes including enhancing performance or maintaining or initiating alertness.

There are a great variety of such agents. These agents run the gamut from stimulants such as caffeine to drugs such as analgesics, tranquilizers, cardiovascular products, insulin, etc. Some such agents are taken on an as needed basis while other agents must be taken at regular intervals by the individual.

Typically, drugs (medicaments) are administered parenterally or enterally. Of course, parenteral administration is the administration of the drug intravenously directly into the blood stream. Enteral refers to the administration of the drug into the gastrointestinal tract. In either case, the goal of the drug administration is to move the drug from the site of administration towards the systemic circulation.

Except when given intravenously, a drug must traverse several semipermeable cell membranes before reaching general circulation. These membranes act as a biological barrier that inhibits the passage of drug molecules. There are believed to be four processes by which drugs move across a biological barrier: passive diffusion; facilitated diffusion; active transport; and pinocytosis.

Passive diffusion is the transport across the cell membrane wherein the driving force for the movement is the concentration gradient of the solute. In orally administered drugs, this absorption occurs in the small intestines. Facilitated diffusion is believed to be based on a carrier component that combines reversibly with the substrate molecule at the cell membrane exterior. The carrier substrate complex diffuses rapidly across the membrane with release of the substrate at the interior surface. Active transport requires an energy expenditure by the cell and appears to be limited to agents with structural similarities to normal body constituents. These agents are usually absorbed from specific sites in the small intestines. Pinocytosis refers to the engulfing of particulars or fluid by a cell. It is believed to play a minor role in drug transport. *Merck Manual*, 16th Edition, pp. 2598-2599.

In determining the efficacy of a drug and the effectiveness of the use of a drug to treat a disease, drug absorption is a critical concern. Drug absorption refers to the process of drug movement from the site of administration toward the systemic circulation.

Oral administration of drugs is by far the most common method. When administered orally, drug absorption usually occurs due to the transport of cells across the membranes of the epithelial cells within the gastrointestinal tract. Absorption after oral administration is confounded by numerous factors. These factors include differences down the alimentary canal in: the luminal pH; surface area per luminal volume; perfusion of tissue, bile, and mucus flow; and the epithelial membranes. See *Merck Manual* at page 2599.

A further issue effecting the absorption of orally administered drugs is the form of the drug. Most orally administered drugs are in the form of tablets or capsules. This is primarily for convenience, economy, stability, and patient acceptance. Accordingly, these capsules or tablets must be disintegrated or dissolved in the stomach before absorption can occur. There are a variety of factors capable of varying or retarding disintegration of solid dosage forms. Further, there are a variety of factors that effect the dissolution rate and therefore determine the availability of the drug for absorption. See *Merck Manual* at page 2600.

Parenteral administration allows for the direct placement of the drug into the blood stream. This usually ensures complete delivery of the dose to the general

circulation. However, administration by a route that requires drug transfer through one or more biologic membranes to reach the blood stream precludes a guarantee that all of the drug will eventually be absorbed. Even with parental administration, because capillaries tend to be highly porous, the perfusion (blood flow/gram of tissue) is a major factor in the rate of absorption. Thus, the injection site can markedly influence a drugs' absorption rate; e.g., the absorption rate of diazepam injected IM into a site with poor blood flow can be much slower than following an oral dose. See *Merck Manual* at page 2601.

Not only is drug absorption an issue in drug delivery but, the bioavailability of the drug is also critical. Bioavailability is defined as the rate at which and the extent to which the active moiety (drug or metabolite) enters the general circulation, thereby gaining access to the site of action. Bioavailability depends upon a number of factors, including how a drug product is designed and manufactured, its physicochemical properties, and factors that relate to the physiology and pathology of the patient. See *Merck Manual* at page 2602.

When a drug rapidly dissolves from a drug product and readily passes across membranes, absorption from most site administration tends to be complete. This is not always the case for drugs given orally. Before reaching the vena cava, the drug must move down the alimentary canal and pass through the gut wall and liver, which are common sites of drug metabolism. Thus, the drug may be metabolized before it can be measured in the general circulation. This cause of a decrease in drug input is called the first pass effect. A large number of drugs show low bioavailability owing to an extensive first pass metabolism. The two other most frequent causes of low bioavailability are insufficient time in the GI tract and the presence of competing reactions. See *Merck Manual* at page 2602.

Bioavailability considerations are most often encountered for orally administered drugs. Differences in bioavailability can have profound clinical significance.

Although parenteral administration does provide a method for eliminating a number of the variables that are present with oral administration, parenteral administration is not a preferable route. Typically, parenteral administration requires the use of medical personnel and is just not warranted nor practical for the

administration of most agents and drugs, e.g., analgesics. Even when required parenteral administration is not preferred due to patient concerns including comfort, infection, etc., as well as the equipment and costs involved. However, despite best efforts certain therapies require parenterally injected drugs. For example, research for decades has focused on an attempt to deliver insulin to an individual through a non-parental means. Despite such efforts today insulin is still only administered intravenously.

There is therefore a need for an improved method of delivering drugs and agents to an individual.

SUMMARY OF THE INVENTION

The present invention provides improved products and methods for delivering a medicament or agent to an individual. Improved formulations including medicaments or agents are also provided by the present invention.

To this end, the present invention provides a product including a medicament comprising a consumable center and a compressible composition including a medicament that is compressed around the consumable center. The medicament may be encapsulated.

The chewable consumable center can be, by way of example and not limitation, a gummi candy, confectionary starch, hard candy, licorice-type candy or tableted excipient such as dextrose, sucrose, or other saccharides, sorbitol, mannitol, isomalitol, other sugar alcohols, or combinations thereof.

In an embodiment, the product has a disk shape.

In an embodiment, the product has a pellet shape.

In an embodiment, the product has a spherical shape.

In an embodiment, the product has a cube shape.

In an embodiment, the encapsulated medicament is encapsulated with a composition selected from the group consisting of: natural polymers; synthetic polymers; modified cellulosics; and protein.

In an embodiment, the consumable center has the same shape as the product.

In an embodiment, the medicament is selected from the group consisting of: analgesics; muscle relaxants; antacids; antihistamines; decongestants; anti-

inflammatories; antibiotics; anti-virals; psycotherapeutic agents; hormones; cardiovascular agents; vitamins; minerals; and nutriceuticals.

In an embodiment, the compressible composition includes a masking agent.

In an embodiment, the consumable center is chosen from the group consisting of gummi candy, hard candy, confectionary starch, or compressible excipient.

In another embodiment of the present invention, a composition including a medicament is provided comprising a consumable center and a compressible formulation including a medicament that surrounds the entire consumable center.

In an embodiment, the medicament is encapsulated. To this end, the medicament can be encapsulated with a composition selected from the group consisting of: natural polymers; synthetic polymers; modified cellulosics; and protein.

In an embodiment, the medicament is selected from the group consisting of: analgesics; muscle relaxants; antacids; antihistamines; decongestants; anti-inflammatories; antibiotics; anti-virals; psycotherapeutic agents; hormones; cardiovascular agents; vitamins; minerals; and nutriceuticals.

In a further embodiment of the present invention, an acetominophen containing product is provided comprising a consumable center and a compressible composition including encapsulated acetaminophen, the compressible composition is compressed around the consumable center.

In yet another embodiment of the present invention a method of delivering a medicament is provided comprising the steps of: providing a consumable center; compressing around the consumable center a composition including a medicament; and causing an individual in need of the medicament to chew the product.

In an embodiment, the medicament is encapsulated.

In an embodiment, the medicament is selected from the group consisting of: analgesics; muscle relaxants; antacids; antihistamines; decongestants; anti-inflammatories; antibiotics; anti-virals; psycotherapeutic agents; hormones; cardiovascular agents; vitamins; minerals; and nutriceuticals.

Still further, in an embodiment, the present invention provides a method for providing a medicament comprising the steps of: providing a consumable center; and compressing around the chewing gum center a composition including a medicament.

Additionally, the present invention provides a method of producing a medicament containing product comprising the steps of: producing a consumable center; and surrounding the consumable center with a powder that includes a medicament.

Accordingly, an advantage of the present invention is to provide new methods for delivering medicaments to an individual.

Furthermore, an advantage of the present invention is to provide improved products containing a medicament.

Still further, an advantage of the present invention is to provide a method of delivering medicaments to an individual that provides for increase absorption and bioavailability as compared to medicaments that are designed to be absorbed in the GI tract.

Another advantage of the present invention is to provide a novel method of delivering medicaments to an individual that provide relief from pain symptoms.

Further, an advantage of the present invention is to provide chewable products containing medicaments that have excellent content uniformity.

Still, an advantage of the present invention is to provide a method of delivering medicaments that does not require the individual to take water.

Moreover, an advantage of the present invention is to provide a method for administering medicaments to an individual that heretofore were administered parentally.

Additionally, an advantage of the present invention is to provide a method for administering medicaments that is more palatable than current methods.

Another advantage of the present invention is to provide an improved method for drug delivery.

An additional advantage of the present invention is that it can provide an acetaminophen containing product that can be chewed and is palatable.

Further, an advantage of the present invention is that a chewable product including medicament is provided that can have a variety of shapes.

Additional features and advantages of the present invention will be described in and apparent from the detailed description of the invention and the figures.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 illustrates generally an embodiment of the product of the present invention.

Figure 2 illustrates graphically the results of Experiment No. 1 that is discussed supra.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides improved methods for delivering medicaments and other agents to an individual as well as improved products including such medicaments or agents.

Pursuant to the present invention, a medicament is contained in a compressible formulation that surrounds a consumable center. As used herein "consumable center" means that a center is provided that can be ingested by the consumer. Preferably, the center can be chewed by the consumer. Unlike chewing gum, the consumable center is designed to dissolve in the mouth of the consumer and/or to be swallowed. If desired, the center can be tableted so that it has a precise size (within an acceptable range) depending on the medicament or agent and shape. This allows an accurate control of the coating as well as allows one to produce products having specific sizes and shapes. In an embodiment, the coating comprises at least 50% by weight of the entire product.

As the product is chewed or crushed in the mouth of the consumer, the medicament is released into the saliva. During continual chewing, the medicament in the saliva is then forced through the oral mucosa in the buccal cavity due to the pressure created by the chewing. The oral mucosa has a thin epithelium and a rich vascularity. Thus, the oral mucosa favors drug absorption. In contrast to a typically orally ingested drug, wherein the solution is in contact too briefly for absorption to be appreciable through the oral mucosa, it is believed that during chewing, the agent and/or medicament remains in the buccal cavity and is forced through the oral mucosa. Also it has been surprisingly found that an increase in the absorption of the drug is achieved as well as an increase in the bioavailability of the drug as compared to typical oral administration. It has been found that the medicament is absorbed much quicker than if it was swallowed as in a typical oral administration. Indeed, the absorption

may in certain cases approach that of a parenteral administration, and the bioavailability is much greater than oral administration.

Referring to Figure 1, an embodiment of the product 10 of the present invention is illustrated. As illustrated, the product 10 includes a consumable center 12. The consumable center 12 can be any of a variety of confectionery products or compressible excipients known in the art. Such confectionery products that are consumable include, without limitation, gummi candies, hard candies, confectionery starches and licorice-based candies. Examples of compressible excipients include, without limitation, saccharides such as dextrose and sucrose, and sugar alcohols such as sorbitol and mannitol, and combinations of same.

Pursuant to the present invention, surrounding the consumable center 12 is a compressed powder 14. The compressed powder 14 is a compressible formulation that is compressed around the consumable center 12, and includes a medicament or other active agent. It should be noted, if desired, the consumable center can also include medicaments.

By using a compressible formulation including a medicament, a variety of shapes and products can be provided. In the preferred embodiment illustrated in Figure 1, a disk shaped product 10 is provided. However, any geometry can be created, including cubes, pellets, ovals, and spheres. Further, if desired, indicia can be stamped onto the compressed powder 14 and thereby the product 10.

It should be noted that the consumable center 12 can either be completely encased by the compressed powder 14 or it may be partially exposed. Further, the consumable center 12 may either have the same shape as the compressed powder 14 and the product 10 or it can have a different shape. For example, a spherical consumable center can be utilized with an oval compressed product.

Pursuant to the present invention, a compressible formulation, powder, is compressed around the consumable center in order to form the product. This provides advantages over creating products that may be coated with a medicament. In this regard, typically chewing gum coatings are created by a pan coating process. The present invention provides a number of advantages over the pan coating processes. Pan coating processes typically allow for less than 200 mg/piece of the active agent. There can also be processing control and dosing issues with respect to products produced

using current pan coating processes. Further, pan coated procedures may create stability and shelf life issues with respect to the resultant product.

By utilizing a compressible powder for creating a tableted product, excellent content uniformity can be provided. For example, in an embodiment, it has been found that a product can be provided that will have ± 3.1 % at 300 mg dosage which is ± 10.9 mgs.

As noted above, the compressible powder includes a medicament. The medicament can be blended with a powder to create the compressed powder through a variety of methods. The blending may be performed by a standard mixing means, using a Vee Blender, a Ribbon Blender or other mixer. The powder is formulated to provide a compressible matrix, using bulk fillers, sorbitols, sugars, polyols, starches, sugars modified with starches and the like. Preferably, this filler can range from approximately 10 to about 95% by weight composition of the powder and active/medicament blend. Preferably the active/medicament may range from approximately 0.001 to about 60% by weight of the powder and active/medicament blend. Other components that can be present in the powder include flavors, colors, sweeteners and high potency sweeteners. Other excipients can also be used in the powder that are useful in modifying mouthfeel and organoleptic properties of the product. Excipients may also be used to modify dissolution and disintegration properties and binding of the product. Preferably the weight of the powder and active/medicament blend may range from approximately 10 to about 90% weight of the total product.

As noted above, if desired, the medicament can be encapsulated or it can be free. In order to produce the encapsulated medicament, a variety of technologies can be utilized. For example, film coating technologies can be used to provide effective taste masking of a pharmaceutical agent. A number of materials can be utilized to encapsulate the medicament including, natural polymers, synthetic polymers, modified cellulose, waxes, fats, oils, and proteins. In addition, a diverse range of modifiers can be used, including, but not limited to, plasticizers, pore formers, disintegrants, waxes, lipids, fats, fatty acids, polylactides, solubilizers, and absorption enhancers.

Several encapsulating techniques can be used to encapsulate the medicament. These include fluid-bed coating and its variations, low-shear wet granulations, high-

shear wet granulations, and spray dry processes. The encapsulations provide for coated solid particles and matrix dispersions. This enhances bioavailability, taste masking, and tailored release profiles. It has been found that high-shear granulations of active powder with modifying agents provide for taste masking, absorption enhancement, dissolution aides, and mouth feel modifiers. The tailored release profile focuses on the immediate release of a pharmaceutical/active, a standard delivery profile of pill forms of medicaments/actives and delayed or sustained release of a pharmaceutical active as given by entreric coating processes.

The compressed powder can include masking agents. In this regard, high-intensity sweeteners and appropriate flavors can be used to mask any off notes that are present due to the medicament or agent. It has been found that with respect to certain medicaments or agents that may have an astringent or bitter taste that by adding a masking agent to the formulation, that a much more palatable formulation, including the medicament, can be provided.

The masking agents, in an embodiment, are selected from the group consisting of sucralose; zinc gluconate; ethyl maltol; glycine; acesulfame-k; aspartame; saccharin; fructose; xylitol; maltitol; cooling agents; isomalt; salt; spray dried licorice root; glycyrrhizin; dextrose; sodium gluconate; sucrose; glucono delta-lactone; ethyl vanillin; and vanillin.

In an embodiment of the invention, sufficient masking agent will be used in the compressed powder to improve and provide acceptable organoleptic properties to the chewing gum product. As used herein to provide "acceptable organoleptic properties" means that the product will have a sufficiently pleasant, or at least non-offensive taste, to allow the consumer to chew the product for a sufficient time to allow the medicament to be released into the buccal cavity. Whether a masking agent is necessary and/or the amount of masking agent will vary depending on medicament. Of course, if desired, more than one masking agent can be used, e.g., zinc gluconate and a sweetener or flavor. In an embodiment, the masking agent may comprise approximately 10% to about 90°/o by weight of the powder formulation.

In a preferred embodiment, the compressed powder includes a high-intensity sweetener such as aspartame, sucralose, and acesulfame-k. In an embodiment, the

high-intensity sweetener comprises approximately 0.5% to about 5% by weight of the coating.

The core, center of the product is a consumable product that can be chewed or crushed. It has been found that this component of the present invention reduces any aftertaste that may be present from the medicament. The consumable center also speeds delivery of the drug by increasing production of saliva. The increase in saliva assists in swallowing the medicament without drinking water. Further an increased absorption is achieved through oral mucosa by creating fluid pressure.

The compression of the powder and medicament blend around the consumable center can be performed by modifying existing tableting equipment presently used in the pharmaceutical industry. For example, a modification can be made to equipment as the Single Layer or Multilayer Rotary Tablet Press, to include placement of a core, prior to final compression. The powder blend will then surround the consumable center and is mechanically compressed to form the final product.

It has also been surprisingly found that by placing a medicament in an powder that is compressed around a consumable center less medicament or agent can be placed in the product than is typically orally administered to an individual to achieve an effect and the same bioequivalence can be achieved. In fact, it has been surprisingly found that in certain instances, for at least certain drugs and agents, the administration of the medicament or agent using chewing gum through the buccal cavity can provide an increase effect even as compared to parenteral administration.

It is envisioned, that a variety of different medicaments and agents can be placed in the compressed powder. Generally, such medicaments include, inter alia, analgesics, antibiotics, antivirals, antihistamines, anti-inflammatories, cancer chemotherapies, antimycotics, oral contraceptives, diuretics, antitussives, anesthetics, nutraceuticals, bioengineered pharmaceuticals, oral vaccines, probiotics, decongestants, antacids, muscle relaxants, psychotherapeutic agents, hormones, insulin, vitamins, and minerals and cardiovascular agents. For example, such agents include, inter alia, stimulants such as caffeine. It is envisioned, that depending on the medicament, the resultant chewing gum can be used to treat, inter alia: coughs; colds; motion sickness; allergies; fevers; pain; inflammation; sore throats; cold sores; sinus problems; diarrhea; diabetics; depression; anxiety; and other maladies and symptoms.

Specific agents/medicaments include, by way of example and not limitation: caffeine; aspirin; acetaminophen; ibuprofen; hydroxycitric acid; antacids; chromium picolinate; phosphatidylserine; nicotine (for smoking cessation); insulin; Echinacea purpurea; zinc; vitamin C; ginseng; kola nut; kaua kaua; and chamomile.

In an embodiment, the medicaments are contained in the compressed powder coating of the product at levels of approximately 50 micrograms to 500 milligrams. The specific levels will depend on the active ingredient. The level of medicament or agent in the compressed powder of the product is selected so as to create, when the product is chewed, a sufficiently high concentration of the medicament or agent in the saliva.

In an embodiment of the present invention, the product includes encapsulated acetaminophen. Preferably the product includes at least 250 mg of acetaminophen and in an embodiment 500 mg. It has been found that the acetaminophen is quickly released from the product into the saliva of the individual chewing the product.

Pursuant to the present invention, depending on the medicament, the dosing regiment will change. For example, if the medicament is an analgesic, the product would be taken on an as needed basis. Of course, similar to the oral administration of an analgesic, there would be restrictions on the number of pieces of product, chewed, for example, not more often than one stick every four hours and not more often than four to five times a day.

By way of example, and not limitation, examples of some coated consumable formulations including a medicament or agent are as follows:

EXAMPLES

Examples of formulations follow.

PRODUCT

The product will include a center and a coating. By way of example, embodiments of the center are as follows:

Center Formulation

Formulation No. 1

INGREDIENTS	WEIGHT USED LBS	DRY WEIGHT LBS	% FINISHED PRODUCT
Dry Sugar	6.00	6.00	59.23
Water	3.00		
Corn Syrup 42DE, 43 BE	5.00	4.00	39.52
Yellow Color	TO SUIT	--------	
Citric Acid	56 gr	0.12	1.25
Lemon Flavor	5 ml.	--------	--------
TOTAL	14.12	10.12	100.00

Manufacturing Procedure:

Weigh the ingredients. Place the sugar, water, corn syrup, and color in an open fire pan and wash the sides down with the water. Cook the batch to 280°F. Transfer the batch to the vacuum cooker. Turn on the vacuum pump and draw 27" of vacuum. Hold the vacuum at 27" for four minutes. Vent the vacuum kettle and open the pan to empty the unit. Scrape the batch into a transfer pan and place it on the cooling slab. Cool and temper the batch while mixing in the flavor and acid. Hand spin and cut into bite sized pieces using the wafer cutter. Cool the candy and pack.

Formulation No. 2

Ingredients	Weight for 1500 gm finished product
Rousselot® 250 A, gelatin 30 mesh	90 gm
Corn syrup 42 DE	675 gm
Granulated sugar	555 gm
Water (for gelatin solution)	180 gm
Water (for sugar solution)	210 gm
Citric Acid solution (50%)	30 gm

Manufacturing Procedure:

Depending on mesh size of the Rousselot® gelatin, allow it to swell in cold water or dissolve directly in water heated to 80-90°C (176-194°F). Boil granulated sugar, corn syrup and remainder of water to 116°C (241°F). Cool to 100°C (212°F).

Add gelatin solution either swollen or as a solution. Stir slowly (until swollen gelatin has completely dissolved) in order to produce a homogeneous mixture. Use deaerating equipment to remove air bubbles from the mixture or allow mixture to stand at 80°C (176°F) until a thin film forms at the surface. Remove film prior to depositing. Add citric acid, flavor and color. Deposit in cool, dry starch (maximum 30-35°C or 86-95°F and 6-8% moisture). Sprinkle some starch on top of the candies. Depositing solids should be 77-78 brix. Depositing temperature should be 70-75°C (158-167°F). Store starch trays overnight at room temperature. After removal from starch, either oil or sugar sand candies. The texture of the finished candies can be modified by adjusting gelatin usage level or bloom strength.

FORMULATION #3 (Sweetose 64 D.E. Syrup)

SWEETOSE 4300	143.0 lb
Granulated Sugar	100.0
MIRA-QUIK MGL Starch	11.5
Confectioners G Starch	20.0
Water	215.0
	489.5

FORMULATION #4 (42 D.E. Syrup)

Staley 1300 Corn Syrup	107.0 lb
Crystalline Dextrose	36.0
Granulated Sugar	100.0
MIRA-QUIK MGL Starch	11.5
Confectioners G Starch	20.0
Water	215.0
	489.5

Procedure (either formula):

Mix the starch into 125 lbs of water and set aside. Add the remaining water and sweeteners to the cooking kettle and heat to boiling. Then slowly add the starch slurry and cook to about 226°F (or 78% solids). Add color and flavor and deposit into moulding starch. Dry to a minimum 80% solids (24 hours at 120-140°F). Shake out and sugar sand.

Formulation No. 5

Ingredient	Percent of Uncooked Mix
Corn Syrup - 63 D.E.	47.00
Flour - Wheat	25.00
Sugar	12.50
Water	7.00
Corn Starch	6.00
Partially Hydrogenated Vegetable Oil	1.30
Flavor	0.40
Salt	0.30
Citric Acid	0.30
Titanium Dioxide	0.10
Red #40 Dye	0.07
Vanillin	0.03
	100.0

The above formula is for a continuous cooking system. The mix moisture is approximately 20.0%. The finished candy would contain between 15% and 16% moisture.

If the formula were to be kettle cooked, the mix moisture would be increased to approximately 40%. Also, for kettle cooked licorice, a mold suppressing preservative such as potassium sorbate would usually be added at approximately 0.02%.

Coating

Embodiments of powder coating formulations as follows (percentage composition)

Ingredient	Example 6	Example 7	Example 8	Example 9	Example 10
Sorbitol	70.90	—	—	63.30	—
Dextrose	—	68.30	—	—	60.00
Fructose	—	—	65.00	—	—
Encapsulated Acetaminophen	15.00	—	—	22.60	—
Powder Acetaminophen	—	18.00	—	—	—
Granular Acetaminophen	—	—	20.00	—	—
Granulated Acetaminophen	—	—	—	—	25.00
Polvinyl pyrolidone	—	5.00	—	—	6.50
Microcrystalline Cellulose	6.00	—	5.50	6.00	—
Aspartame	3.00	2.40	2.00	2.40	5.00
Sucralose	1.50	2.00	3.50	1.50	—
WS-23	0.10	0.20	0.30	0.10	0.25

Ingredient	Example 6	Example 7	Example 8	Example 9	Example 10
Calcium Stearate	—	1.00	—	—	0.75
Magnesium Stearate	1.00	—	0.60	1.00	—
Flavor	3.00	3.00	3.00	3.00	2.20
Color	0.10	0.10	0.10	0.10	0.30
Total Percentage	100.00	100.00	100.00	100.00	100.00

The above powder formulations can then be placed around the above consumable centers to make a product.

By way of example, a chewing gum having the formulation:

Ingredient	
Sorbitol	32.30
Base	44.00
Calcium Carbonate	10.00
Maltitol	2.00
Glycerin	4.00
70% Sorbitol Solution	3.50
Flavor	2.50
Menthol	0.50
Granulated Aspartame	0.50
Encapsulated Aspartame	0.50
Acesulfame K	—
Encapsulated Sucralose	—
Citric Acid	—
Lecithin	0.20
Total Percentage	100.00

was coated with Example 9, by using a calibrated volumetric scoop to measure 0.9 grams of powder and poured into the tablet die on a rotary tablet press. The gum center was manually placed on top of the powder and centered, and the volumetric scoop was used to deliver an additional 0.9 gm of coating powder over the gum center. The rotary press was cycled through one full rotation to compress the powder around the gum center.

Experiment No. 1

The aforementioned Example 11 was compared to a pan coated product made in the following manner: Chewing gum ingredients may be mixed in a Sigma Blade Mixer or in a continuous extruding mixer. After mixing, the gum mass is passed through a series of rollers ultimately ending with a pelletizing roller which scored the gum into pieces of the desired shape and size.

The gum centers were loaded into a conventional perforated pan and coated in a manner typical of standard confections. The pellet bed was doused with syrup and allowed to tumble for a period of time to distribute the syrup and dried for another fixed period of time. During the intermediate phases of this process, a dry charge consisting of maltitol and powdered acetaminophen was sprinkled on the moist bed of pellets and incorporated into the pellet coating prior to complete drying. This is repeated as necessary to build up the desired drug dose on the outside of the pellets.

Kinetic analysis was performed on three subjects to determine the amount of acetaminophen, which was chewed into the cud. The comparative examples used were Driam pan coated gum with a 195 mg/pellet of acetaminophen and Driam pan coated gum with 150 mg/pellet of acetaminophen were compared to the experimental samples of Compressed Tablet Chewing Gum with 355 mg/pellet of acetaminophen. The time points taken for the pan coated 195 mg/pellet product were at 0, 2, 5, 10 and 20 minutes. Time points for the 150 mg/pellet product were at 0, 10, 20, 30, and 40 minutes. The time points taken for the Compressed Tablet Chewing Gum 355 mg/pellet product were 0, 1, 3, 5, 8, 14, and 20 minutes.

Figure 2 illustrates graphically the results of this analysis.

It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the present invention and without diminishing its intended advantages. It is therefore intended that such changes and modifications be covered by the appended claims.

WE CLAIM:

1. A product including a medicament comprising:

a consumable center; and

a compressible composition comprising an encapsulated medicament that is compressed around the consumable center.

2. The product of Claim 1 wherein the product has a disk shape.

3. The product of Claim 1 wherein the product has a pellet shape.

4. The product of Claim 1 wherein the product has a spherical shape.

5. The product of Claim 1 wherein the product has a cube shape.

6. The product of Claim 1 wherein the encapsulated medicament is encapsulated with a composition selected from the group consisting of: natural polymers; synthetic polymers; modified cellulosics; waxes; fats; oils; and protein.

7. The product of Claim 1 wherein the consumable center is selected from the group consisting of gummi candy, confectionary starch, hard candy, licorice-type candy and tableted excipients.

8. The product of Claim 1 wherein the medicament is selected from the group consisting of: analgesics; muscle relaxants; antacids; antihistamines; decongestants; anti-inflammatories; oral vaccines; probiotics; antibiotics; anti-virals; cancer chemotherapies; antimycotics; oral contraceptives; diuretics; antitussives; anesthetics; bioengineered pharmaceuticals; psycotherapeutic agents; hormones; cardiovascular agents; vitamins; insulin; minerals; and nutraceuticals.

9. The product of Claim 1 wherein the compressible composition includes a masking agent.

10. A composition including a medicament comprising:

a consumable center; and

a compressible formulation including a medicament that surrounds the entire consumable center.

11. The composition of Claim 10 wherein the medicament is encapsulated.

12. The composition of Claim 10 wherein the composition has a disk shape.

13. The composition of Claim 10 wherein the medicament is encapsulated with a composition selected from the group consisting of: natural polymers; synthetic polymers; modified cellulosics; waxes; fats; oils; and protein.

14. The composition of Claim 10 wherein the medicament is selected from the group consisting of: analgesics; muscle relaxants; antacids; antihistamines; decongestants; anti-inflammatories; antibiotics; anti-virals; oral vaccines; probiotics; psycotherapeutic agents; hormones; cardiovascular agents; vitamins; minerals; insulin; and nutraceuticals.

15. The product of Claim 10 wherein the consumable center is selected from the group consisting of gummi candy, confectionary starch, hard candy, licorice-type candy and tableted excipients.

16. An acetominophen containing product comprising:

a consumable center; and

a compressible composition including encapsulated acetaminophen that is compressed around the consumable center.

17. The acetominophen containing product of Claim 16 wherein the product has a disk shape.

18. The acetominophen containing product of Claim 16 wherein the acetominophen is encapsulated with a composition selected from the group consisting of: natural polymers; synthetic polymers; modified cellulosics; waxes; fats; oils; and protein.

19. The acetominophen containing product of Claim 16 wherein the consumable center has the same shape as the product.

20. A method of delivering a medicament comprising the steps of:

providing a consumable center;

compressing around the consumable center a composition including a medicament to produce a product; and

causing an individual in need of the medicament to chew the product.

21. The method of Claim 20 wherein the medicament is encapsulated.

22. The method of Claim 21 wherein the medicament is encapsulated with a composition selected from the group consisting of: natural polymers; synthetic polymers; modified cellulosics; and protein.

23. The method of Claim 20 wherein the product is chewed a plurality of times per day.

24. The method of Claim 20 wherein the medicament is selected from the group consisting of: analgesics; muscle relaxants; antacids; antihistamines; decongestants; anti-inflammatories; antibiotics; anti-virals; oral vaccines; probiotics; cancer chemotherapies; antimycotics; oral contraceptives; diuretics; antitussives; anesthetics; bioengineered pharmaceuticals; insulin; psycotherapeutic agents; hormones; cardiovascular agents; vitamins; minerals; and nutraceuticals.

25. The method of Claim 20 wherein the medicament is acetominophen.

26. The product of Claim 20 wherein the consumable center is selected from the group consisting of gummi candy, confectionary starch, hard candy, licorice-type candy and tableted excipients.

27. A method for providing a medicament comprising the steps of:

providing a consumable center; and

compressing around the consumable center a composition including a medicament.

28. The method of Claim 27 wherein the medicament is encapsulated with a composition selected from the group consisting of: natural polymers; synthetic polymers; modified cellulosics; waxes; fats; oils; and protein.

29. The method of Claim 27 wherein the medicament is selected from the group consisting of: analgesics; muscle relaxants; antacids; antihistamines; decongestants; anti-inflammatories; antibiotics; anti-virals; cancer chemotherapies; antimycotics; oral contraceptives; diuretics; antitussives; anesthetics; oral vaccines; probiotics; bioengineered pharmaceuticals; insulin; psycotherapeutic agents; hormones; cardiovascular agents; vitamins; minerals; and nutraceuticals.

30. The method of Claims 27 wherein the medicament is acetominophen.

31. A method of producing a medicament containing product comprising the steps of:

producing a consumable center; and

surrounding the consumable center with a compressible powder that includes a medicament.

32. The method of Claim 31 wherein the medicament is encapsulated with a composition selected from the group consisting of: natural polymers; synthetic polymers; modified cellulosics; and protein.

33. The method of Claim 31 wherein the medicament is selected from the group consisting of: analgesics; muscle relaxants; antacids; antihistamines; decongestants; anti-inflammatories; antibiotics; anti-virals; cancer chemotherapies; antimycotics; oral contraceptives; diuretics; antitussives; anesthetics; bioengineered pharmaceuticals; psycotherapeutic agents; hormones; cardiovascular agents; oral vaccines; probiotics; insulin; vitamins; minerals; and nutraceuticals.

34. The method of Claim 31 including the step of compressing the powder around the consumable center.

35. The product of Claim 31 wherein the consumable center is selected from the group consisting of gummi candy, confectionary starch, hard candy, licorice-type candy and tableted excipients.

FIG.1

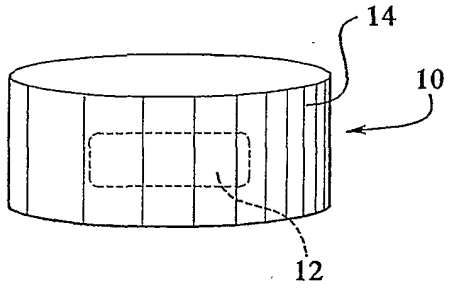
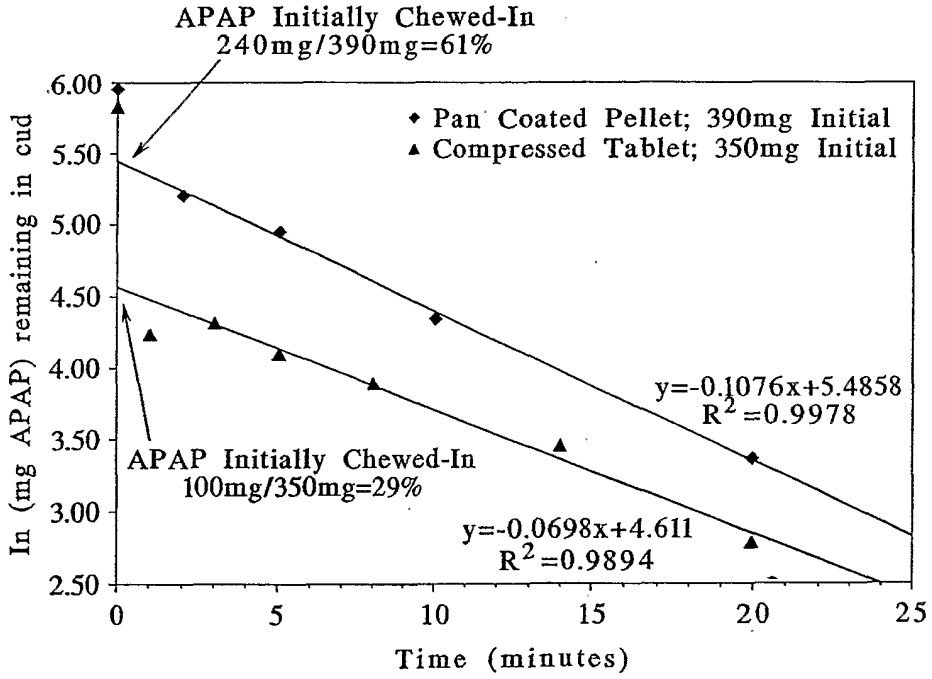

14
10
12

FIG.2


APAP Initially Chewed-In
240mg/390mg=61%
Pan Coated Pellet; 390mg Initial
Compressed Tablet; 350mg Initial
y=-0.1076x+5.4858
R2=0.9978
APAP Initially Chewed-In
100mg/350mg=29%
y=-0.0698x+4.611
R2=0.9894
In (mg APAP) remaining in cud
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
0
5
10
15
20
25
Time (minutes)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/20038

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A 61K 9/20; 9/68
US CL : 424/48, 440, 464, 465; 426/5

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/48, 440, 464, 465; 426/5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
USPATENTS, USPG-PUB, DERWENT, EPO

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6,355,265 B1 (REAM et al) 12 March 2002 (12.03.2002), entire document	1-35
A	US 6,290,985 B2 (REAM et al) 18 September 2001 (18.09.2001), entire document.	1-35
A	US 6,426,090 B1 (REAM et al) 30 June 2002 (30.06.2002), entire document.	1-35
A	US 6,322,806 B1 (REAM et al) 27 November 2001 (27.11.2001), entire document.	1-35
A	US 5,665,406 A (REED et al) 09 September 1997 (09.09.1997), entire document.	1-35
A	US 5,536,511 A (YATKA) 16 June 1996 (16.06.1996), entire document.	1-35
A	US 2001/0021403 A1 (ZYCK et al) 13 September 2001 (13.09.2001), entire document.	1-35

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 August 2002 (12.08.2002)	12 SEP 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Valerie Bell-Harris for Charesse Evans Telephone No. (703) 308-0196

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