Modified dosage evaluation of continued release of DiDomenico sodium tablets by means of hydrophilic polymer blends

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ABSTRACT

That term altered - discharge measurement manifestation is used to portray results that change the timing and rate for the arrival of the drug substance. A modified release measurement type will be characterized "as a particular case to which the pill arrival aspects for a period course or area need aid picked on finish restorative alternately comfort destinations not advertised by rou- tine measurement structures, for example, solutions, ointments, alternately immediately dissolving dosages manifestations. xanthan gum, a polysaccha- ride, crude cashew gum, Diclofenac sodium powder, hydroxypropyl methyl- cellulose, microcrystalline cellulose, talc and magnesium stearate. Wet granu- lation, procedure of wet granulation in 6-Step. Every last one of batches of tablets passed that consistency and weight test and pill substance test the batches of tablets be that as clump 3 passed those pulverizing quality test every last one of batches and tablets yet batches 4 furthermore 10 passed the friability test. Tablets holding main xanthan gum similarly as arrival modifier attained the most astounding pulverizing quality friability proportion (CSFR) for the individuals clinched alongside clump 10 hosting those most reduced. Furthermore, the individuals for clump 3 required the most reduced swelling list. Those investigations need demonstrated that cashew furthermore xan- than gums utilized alone can’t proficiently control medication regardless of discharge. Batches 7 and 8 holding xanthan gum also HPMC were capable on the result in supported medication regardless of discharge comparable to Voltaren retard.

INTRODUCTION

Medication results planned to decrease that recurrence and dosing by modifying those rates for pill absorption need be accessible to numerous quite some times there will be general and continuous examine under the utilization about regularly happening biocompatible polymeric materials in the outline about measurement types for oral controlled discharge organization. Those quest to elective results starting with renewable sources need expanded altogether through the considerable length of time. Items that could be used through an in length time will decrease the cosset and import-
ing these fundamental parts that are utilized within the pharmaceutical business. Normally, plant items serve similarly as a great elective on manufactured materials due to neighborhood accessibility, eco-friendliness, also easier fetches contrasted with foreign engineered results (Franz et al., 1987).

Hydrophilic polymers need pulled in respectable consideration for utilization likewise supported and regulated arrival units to this conveyance and both water soluble and water insoluble operators. Their aspects Furthermore capability on hydrate furthermore, manifestation a gel layer are great referred to furthermore vital on support also control pill discharge from matrices. The hydrated gel layer thickness determines those dispersion ways of the medication regardless of particles through those polymer impostors under those dissemination media. Gums would characteristic exudates starting with those bark and trees; furthermore, they need been of incredible pharmaceutical importance. Plant polysaccharides are helpful to that development of drug conveyance frameworks to particular drug conveyance. A percentage regular gums e. G. Guar, tamarind, insect bean, furthermore okra gums likewise polymeric materials bring been showed up for be suitableness in the outline and controlled drug conveyance frameworks due to their swelling alternately permanganic corrosive profiles (Harland et al., 1988).

A few methodologies have been used to get regulated medication release, yet the hydrophilic grid is distinguished by the simplest and the majority broadly utilized strategy. Upon ingestion of a hydrophilic grid tablet, medication regardless of arrival effects at first from swelling which reasons An gel layer to structure on the tablet surface. This gel layer retards further entrance for liquid furthermore resulting in medication discharge. Those swelling of the polymer grid exceptionally regularly happen with also both and they help those generally speaking rate and medication discharge. The utilization and hydrophilic gum blends as the hydrophilic grid might further a chance to be investigated to determine if this arrival of the dynamic element could be regulated further.

A few gum blends bring been explored under and the utilization of a mix and xanthan and cashew gums will be investigated. Hydrophilic polymers need aid broadly utilized within those plans about modified release oral measurement structures. Their accommodation and straightforwardness and assembling might chop down those cosset of the last item. Besides, that hydrophilic polymer grid framework offers a few extra preferences In different advances for regulated arrival pill conveyance. The instrument and the impact of different innovative unrest and detailing variables on the medication regardless of arrival from hydrophilic frameworks need been greatly concentrated on. Until now, an expansive number about regular and manufactured polymers, single alternately clinched alongside combinations, bring been recorded as hydrophilic grid excipients (Baveja et al., 1989).

Prologue and grid tablet by sustained release need provided for a leap forward to novel drug conveyance frameworks in the field and pharmaceutical innovation organization. It excludes unpredictable generation methods, for example, covering furthermore pelletization throughout the manufacturing and the pill arrival rate from that measurement structure is controlled principally by those sort also extent about polymer utilized within those arrangements. Due to expanded muddling furthermore liability included in the promoting of new drug entities, researchers bring centered more excellent consideration on the advancement and sustained-release alternately regulated arrival pill conveyance frameworks.

Maintained Release

Incorporates whatever medication conveyance framework that accomplishes moderate arrival of the medication over a broadened time. The greater part sustained-release formulations need aid planned with the goal that the organization of an absolute measurement unit gives those prompt discharge and a sum medication regardless that immediately produces the fancied restorative impact also gradual and consistent arrival for extra sums of the pill with look after this level about impact through a developed time generally eight should take twelve hours (Banker and Rhodes, 1990).

Figure 1: Plasma medication centralization profiles.

Figure 1 Plasma medication centralization profiles for traditional tablet formulation, a sustained release detailing also a zero request controlled discharge detailing. Controlled and maintained arrival
need both been utilized inconsistently furthermore confusingly. Both representable a differentiate conveyance procedure. Maintained arrival constitutes any measurement structure that gives prescription through an enlarged chance or means that the framework could provide a few genuine restorative control if this may be temporal, spatial nature, alternately both. Supported discharge frameworks by don’t accomplish zero-order kind discharge and normally attempt will emulate zero-order discharge by giving medications done. A moderate initial request (Karasulu, 2000). Repeatable movement tablets need aid an elective system for supported arrival done which various doses for medications need aid held inside An measurement structure also every dosage is discharged toward occasional intervals.

Delayed release system, clinched alongside contrast, might not make sustained, since frequently all those work of these measurement manifestations is to uphold the medication in the measurement for a percentage period preceding release, to example, enteric coated tablets. Those perfect gas method for giving a correct sum and pill toward those sites for the activity to an exact time is as a rule approximated by most frameworks. This close estimation may be attained by making a consistent fixation in the muscle to or an organ in a stretched out time; to different words, the measure for pill entering this framework is equal of the add up for medication regardless evacuated from the framework. At types of digestion system also discharge need aid incorporated in the evacuation process: urinary excretion, enterohepatic recycling, sweat, fecal, et cetera. Since to practically of the medications these disposal techniques need aid initial order; it could a chance to be said that in a sure blood level, the medication will need a particular rate about disposal. That clue should convey the medication during this accurate rate for a broadened time. This is quelled mathematically as takes after, (Pham and Lee, 1994).

\[
\text{Rate in} = \text{Rate out} = \text{kelim} \times \text{Cd} \times \text{Vd}
\]

Eventually, Tom’s perusing those supported discharge method, therapeutically viable focus might be attained in the systemic dissemination again an enlarged period, accordingly accomplishing preferred consistence for patients. Various sustained release oral measurement structures, for example, membrane controlled systems, matrices with water soluble/insoluble polymers alternately waxes, and osmotic frameworks bring been created. Powerful exploration needs as of late concentrated on the designation about sustained release frameworks to poorly water soluble pills. Different pill conveyance strategies have been created on manage this arrival of drugs, including triple-layered tablets and osmotic pumps with laser drilled gaps. These innovations would multi facetted and moderately unreasonable on fabricate. Thus, there remains an enthusiasm toward creating novel formulations that consider the managed discharge of pills utilizing promptly available, modest excipients.

**Xanthan gum is typically utilized**

Likewise, sustenance added substance furthermore, rheology modifier. It is utilized as a nourishment thickening agenize furthermore by a stabilizer. Cashew will be promptly accessible to Ghana and the vast majority regularly utilized a feature may be the nuts that need aid utilized Similarly as nourishment ingredients, yet the gum might a chance to be acted around also misused for utilize in the pharmaceutical industry. The fundamental thought behind the utilization of the grid framework will be on support a consistent level and medication in the blood plasma. Despite the pill doesn’t experience deterioration. This may be exceptionally of service The point when a maintained impact about diclofenac sodium is required for quite a while will treat an incessant portion states such as rheumatoid arthritis, osteoarthritis, constant pain, ankylosing spondylitis and actinic keratosis (Reynolds et al., 1998; Tahara et al., 1995).

**MATERIALS AND METHODS**

**Materials**

Xanthan gum, a polysaccharide, resulting by the microbial coat of xanthomonas campestris was obtained from the Biochemical Store of the Department of Pharmaceutics, KNUST, Kumasi. Crude cashew gum is gotten by the Wenchi Cashew nut estate as natural exudation by the stem bays of the plant Anacardium occidentalis, intimate, Anacardiaceaeat Wenchi in the Brong Ahafo region of Ghana. The plant was authenticated by the custodian of the plantation. Other materials utilized comprises diclofenac Sodium powder (Hubei Prosperity...
### Table 1: Ratios of polymers utilized in the preparations.

| Batch | Formulation | Cashew gum | Xanthan gum | HPMC |
|-------|-------------|------------|-------------|------|
| 1     | C           | 100        | -           | -    |
| 2     | X           | -          | 100         | -    |
| 3     | H           | -          | -           | 100  |
| 4     | H8C2        | 20         | -           | 80   |
| 5     | H6C4        | 40         | -           | 60   |
| 6     | H2C8        | 80         | -           | 20   |
| 7     | X8H2        | -          | 80          | 20   |
| 8     | X6H4        | -          | 60          | 40   |
| 9     | X2H8        | -          | 20          | 80   |
| 10    | X8C2        | 20         | 80          | -    |
| 11    | X6C4        | 40         | 60          | -    |
| 12    | X2C8        | 80         | 20          | -    |
| 13    | C6X2H2      | 60         | 20          | 60   |
| 14    | H6X2C2      | 20         | 20          | -    |
| 15    | X6C2H2      | 20         | 60          | 20   |

KEY: C – Cashew gum, X – Xanthan gum and H – Hydroxypropyl Methylcellulose (HPMC).

Galaxy Chemical Co., Ltd., China), Hydroxypropyl Methylcellulose (UK Chemicals, Kumasi), Microcrystalline Cellulose (Amponsah-Effah Pharmaceuticals Ltd., Kumasi). Talc and magnesium stearate is attained by the Chemical Store of the Department of Pharmaceutics, KNUST, Kumasi (Nellore et al., 1998; Eddington et al., 1998).

**Chemicals and reagents**

96% ethanol, diethyl ether, moved hydrochloric acid, refined water might have been gotten starting with those concoction stores of the section of pharmaceutics and the division about pharmaceutical chemistry, a staff of drug store and pharmaceutical sciences, KNUST Kumasi. Sodium hydroxide pellets, phosphoric acid, sodium dihydrogen phosphate and disodium hydrogen phosphate were got starting with a lab. Chem. Ltd. Kumasi.

**Equipment and apparatus**

Eutech pH meter (pH 510, pH/mV/°C meter), porcelain mortar and pestle, analytical balance (Adam Apparatus), UV spectrophotometer (T90 UV/VIS spectrometer, PG Instruments Ltd.), Erweka closure gadget, (Type DT 6, GmbH Heusenstamm, Germany), Erweka Friabilator (USP), Brookfield Viscometer (Brookfield Engineering LabInc., Middleboro, MA, USA), number 4 sintered glass filters, stormer viscometer, retsch laboratory sieves, sartorius electrical balance, whatman filter papers, retsch mechanical shaker, desiccatar, Monsanto tablet hardness tester, single punch tableting machine, electronic vernier calipers, among others were the equipment and apparatus used (Varma et al., 2004; Yang et al., 1998). To a number of the vivacious or recuperating element, tablets contain some unmotivated resources; these would be distinguished as additives or excipients. They might be ordered as stated by the feature they assume in the completed tablet. That principal assembly holds the individuals which help to confer palatable transforming and layering aspects of the plan these incorporate diluents, binders, glidants and furthermore lubricants. The second gathering of included substances aides on provides for extra alluring physical aspects of the completed tablet. Incorporated in this gathering would disintegrate, colors, and so on.

**Diluents**

Every now and again, those single measurement of the animated element is along these lines little. Inactive substances need aid included will expand those heft should aggravate this tablet a useful extent to layering. Diluents utilized to this design incorporate dicalcium phosphate, calcium sulfate, lactose, cellulose, kaolin, manning, dry starch also powdered sugar, microcrystalline cellulose) (Popli and Sharma, 1990; Kumar et al., 1992).

**Binders**

These are operators used to confer durable qualities of the powdered materials. They confer cohesiveness of the tablet plan which ensures the tablet remaining soundness then afterwards layering and additionally enhancing those free flowing qualities by that plan about granules of wanted hardness also extent. Materials regularly utilized similarly as binders incorporate starch, gelatin and sugars.
Table 2: Bulk density measurements of diclofenac sodium granules prepared.

| Batch No | Loose bulk density (g/mL) | Tapped bulk density (g/mL) | Hausner’s Ratio | Compressibility Index (%) | Angle of repose (º) |
|----------|---------------------------|----------------------------|-----------------|---------------------------|---------------------|
| 1        | 0.56                      | 0.59                       | 1.05            | 5.1                       | 30.80±0.006         |
| 2        | 0.45                      | 0.48                       | 1.07            | 6.3                       | 32.41±0.012         |
| 3        | 0.45                      | 0.5                        | 1.11            | 10.0                      | 28.55±0.026         |
| 4        | 0.50                      | 0.53                       | 1.06            | 5.7                       | 31.50±0.076         |
| 5        | 0.50                      | 0.56                       | 1.12            | 10.7                      | 27.11±0.113         |
| 6        | 0.48                      | 0.5                        | 1.04            | 4.0                       | 35.30±0.006         |
| 7        | 0.45                      | 0.5                        | 1.11            | 10.0                      | 26.41±0.017         |
| 8        | 0.50                      | 0.56                       | 1.12            | 10.7                      | 29.60±0.115         |
| 9        | 0.48                      | 0.53                       | 1.10            | 10.4                      | 31.74±0.092         |
| 10       | 0.53                      | 0.59                       | 1.11            | 10.2                      | 30.20±0.010         |
| 11       | 0.48                      | 0.53                       | 1.10            | 9.4                       | 34.86±0.029         |
| 12       | 0.53                      | 0.59                       | 1.11            | 10.2                      | 25.90±0.012         |
| 13       | 0.53                      | 0.56                       | 1.06            | 5.3                       | 33.42±0.006         |
| 14       | 0.45                      | 0.5                        | 1.11            | 10.0                      | 30.65±0.010         |
| 15       | 0.53                      | 0.56                       | 1.06            | 5.3                       | 32.15±0.026         |

Common engineered gums that need been utilized incorporate acacia, sodium alginate, panwar gum, ghatti gum, carboxymethyl cellulose, methylcellulose and polyvinylpyrrolidone. The amount for folio utilized needs a significant impact on the qualities of the compacted tablet. The utilization about a lot of folio alternately excessively solid a folio will settle on a diligent tablet that won’t crumble effectively and will cause unreasonable wear of punches also dies (Hogan, 1989; Bettini et al., 1995).

Glidants

A glidant may be a substance that enhances the stream qualities of a powder mixture. These materials would regularly include in the dry state Exactly in the recent past layering. Colloidal silicon dioxide is the greater part regularly utilized toward generally low focuses (Bettini et al., 1998; Lee and Kim, 1991).

Tablet qualities

Tablets similarly, as a measurement manifestation ought to help specific particular prerequisites. Those diameters, shape, thickness, the precision of dosage, weight, hardness, stability, deterioration time. Furthermore, disintegration need to fit in with specific parameters.

Tablet hardness and friability

This imperviousness of the tablet on chipping, abrasion or breakage under states of storage, transportation, and taking care of in front of utilization relies on ahead its hardness. Hardness determinations would commit for those tablet runs on figure out the requirements for weight conformity on the tableting machine. A tablet property identified with hardness will be friability. This parameter assesses the capacity of the tablet with withstand abrasion previously, packaging, handling, furthermore shipping (Costa and Lobo, 2001).
Consistency of measurement structures

**Tablet Weight**

The volumetric fill of the bite the dust pit determines the weight of the compacted tablet. The weight of the tablet is that amount of the granulation which holds those marked add up of the restorative agen- nize. Those tablet weights must fit in with those set principles, similarly, as in the USP or BP.

**Substance consistency**

Every tablet must hold numerous those proposed drug amount for minimal variety "around the tablets to a clump. The medication amount for every tablet of normal weight is decided analytically furthermore contrasted with guidelines as set in those monographs (Kaushal, 2001).

| Table 3: Optical density of pure Diclofenac Sodium in Phosphate buffer pH 7.5. |
|---------------------------------|------------------|
| Concentration (%w/v)          | Absorbance |  |
| 0.00250                       | 0.760       |  |
| 0.00150                       | 0.438       |  |
| 0.00125                       | 0.356       |  |
| 0.00100                       | 0.274       |  |
| 0.00075                       | 0.165       |  |

**Tablet deterioration**

On make absorbed, a pill substance must try under solution, yet the deterioration test will be a measure just of the time needed under an provided for situated from claiming states for aggregation from claiming tablets should crumble under particles. In the deterioration test, the disintegration test to measuring the time needed to a provided for a rate of the pill substances in a tablet to try under result under a specified set about states may be an in vitro test. It may be exceptional will give acceptable a step towards this assessment of the physiological accessibility of the medication.

**Solidness**

The Strength of the drug substances has investigated the point when creating the plan. A suitableness system for preparation must make picked for those tableting for delicate substances. The Dependability control returns then afterwards generation by occa- sional examination of a put away reference example of creation batches. Tablets, by and large, need a long time span of usability. Those physio-chemical properties of the tablet ought to additionally make concentrated on throughout stockpiling.

**Wet granulation**

Those the vast majority generally uses and the greater part general system for tablet preparation may be the wet granulation technique. Wet granulation will be a procedure about including a fluid folio or cement of the powder mixture. The measure for fluid might make legitimately managed, and over wetting will reason those granules to make excessively awful difficult also under wetting will foundation them to a chance to be excessively delicate furthermore friable. Watery results need those focal point for continuously safer with manage over solvents.

**The technique of Wet Granulation tissue**

**Step 1:** Weighing and mixing - that dynamic ingredient, filler, deterioration agents, are weighed and blended.

**Venture 2:** the wet granulate may be readied by including the fluid binder/adhesive. Cases from claiming binders/adhesives incorporate watery arrangements for corn starch, characteristic gums, for example, acacia and cellulose acetic acid derivation subsidiaries, for example, methylcellulose.

**Venture 3:** screening those clammy impostors under pellets or granules.

**Venture 4:** Drying the granulation.

**Venture 5:** dry screening: then afterwards those granules are dried, pass recipient an screen of a litter span over the one utilized to the wet impos- tor with select granules of uniform span to permit Indeed fill in those kick the bucket pit.

**Step 6:** Lubrication- a dry lubricant, anti-adherent, also glidant is included of the granules whichever Toward dusting again the spread-out granules or toward mixing for those granules. It diminishes rubbing the middle of this tablet and the dividers of the kick the bucket pit. Anti-adherent diminishes staying of Table 1 of the kick the bucket and punch.

**RESULTS AND DISCUSSION**

**Flow properties of diclofenac sodium granules**

This test does not should station tablets, lozenges and chewable tablets. Disintegration for certain tablets, monographs point out consistency for cut- off points for disintegration as opposed deterioration. Since medication regardless of absorption. Also, physiological accessibility rely on upon hosting the medication on a disintegrated state, suitableness disintegration aspects are a paramount property of a palatable Table 2.

**Compression of diclofenac sodium matrix tablets**
Tablet weight = 420 mg
Number of Tablets = 80 tablets per batch (15 batches in all)
Practical yield = 958 tablets

**Excellence regulator tests approved out on tablets**

Uniformity of weight calculation the percentage deviations of the tablets from the mean were calculated using

\[
\text{Percentage deviation} = \frac{A - B}{B} \times 100
\]

where,

A=Initial weight of tablets
B=Average weight of 20 tablets.

**Dissolution profile of diclofenac sodium tablets formulated with different gum ratios**

It is in this manner distinguished that those in vitro tablet deterioration test doesn’t so much bear an association of the in vivo activity of the tablet. Those greatest deterioration occasion when regularly set during 15 minutes for normal tablets also 60 minutes to covered Table 3. Figure 2 calibration curve for diclofenac sodium in phosphate buffer pH 7.5 at a wavelength of 276 nm completely utilized.

**CONCLUSIONS**

All the clumps of tablets finished the consistency of weight assessment and medication content test. Tablets containing just thickener as delivery modifier accomplished the most noteworthypopover quality friability proportion (CSFR) with those in group 10 having the least. Tablets in a clump 2 had the most elevated expanding file and those in cluster 3 had the least growing record. The examination has indicated that cashew and thickeners utilized alone can’t productively control drug discharge. Clumps 7 and 8 containing thickener and HPMC had the option to cause continued medication discharge tantamount to Voltaren Retard. The plan containing xanthan and cashew gums in groups 10, 11, 12 indicated great supported delivery properties like the reference test. Bunches 13 and 15 which contained each of the three mixes were likewise ready to give continued medication discharge like Voltaren Retard. The delivery profile fit the Higuchi condition in a way that is better than the rest; hence medication may have been delivered through the Higuchi model of medication energy. The delivery example ‘n’ decided was somewhere in the range of 0.45 and 0.89; hence the medication is delivered through atypical or non-Fickian dissemination.

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**Conflict of Interest**

The authors declare that they have no conflict of interest for this study.

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