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# STATISTICAL MODELING OF PHYSICAL CHARACTERISTICS OF FAST DISINTEGRATING GLIPIZIDE TABLETS USING POLYMERIC PROPERTIES

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**Abstract**

The purpose of present study was modeling of statistical relationship between physical attributes of fast disintegrating glipizide (GPZ) tablets and physicochemical properties of polymers used therein. Polymers are type of excipients used for achieving the drug delivery to the desired site in safe and effective way. In present research, various physicochemical properties were calculated for three different polymers and subsequently correlated with physical characteristics of GPZ tablets. This resulted into selection of a statistical model with best correlation and minimal error out of several models developed for each characteristic of formulation. Fourier transform infrared spectroscopic studies confirmed the compatibility between GPZ and all polymers. Estimated parameters for GPZ fast disintegrating tablets such as uniformity of weight (0.32 to 0.55 %), GPZ content (98.97 to 101.34 %), hardness (4.01 to 4.32 Kg/cm$^2$) and friability (0.277 to 0.803 %) were found to be within the prescribed official standards. Also, disintegration time (DT) for tablets from all batches (28.00 to 71.33 sec) indicated faster disintegration. Correlation coefficient ($r^2$) of mathematical models developed for friability ($r^2$ =+0.9657), hardness ($r^2$ =+0.9450) and DT ($r^2$ =+0.9292) specified good correlation with significant effect (F-test) of all selected polymeric properties on physical characteristics of tablets. Therefore, such models could be able to quantitatively predict the polymeric properties that should be highly considered while selecting polymer/s in formulation for required physical characteristics. Subsequently, developed models may also assist in deciding composition of formulation without its actual formulation with saving of material, time and cost of industry.

**Keywords:** Disintegration, Physicochemical properties, Polymer, Statistical modelling.

## Introduction

Drug must reach to site of action in sufficient quantity for sufficient time for achieving desired pharmacological effect. Moreover, a good physical appearance and strength is necessary for solid dosage form to improve their handling properties. This is generally achieved with formulating a drug into dosage form with use of suitable polymer or polymer system. Therefore, selection of polymeric composite requires thorough knowledge of physicochemical properties which is the most important step in formulation design work. Such properties play a major role in deciding the wettability, disintegration, dissolution and hence bioavailability of drug from its formulation. These properties are representative of polymeric structure and usually established by experimental studies, however, can be estimated theoretically in terms of molecular descriptors through quantitative structural property relationship (QSPR) approach[1,2]. Based on theoretically calculated properties and their significant relationship with formulation characteristics, a developed statistical model with good quantitative predictability could help in selection of best suited polymer system and hence composition of formulation. Such modeling of formulation characteristics would have considerable impact on future formulation development research with saving of time and cost of industry.

Hence, present investigation was an attempt to build up a mathematical model having high predictive ability for polymer selection based on statistical relationship obtained between physical qualities of tablet and physicochemical properties of polymers used in tablet formulations. For this, a total of three fast disintegrating tablet formulations containing three different polymers with glipizide (alkaline class) as model drug were prepared and subsequently evaluated for various post-compression parameters.

## Materials and Methods

### Materials

GPZ was obtained from USV Limited (Chiplun, Maharashtra, India) as kind gift sample. Crospovidone (CPVP, S.D. Fine-Chem Ltd., Mumbai, Maharashtra, India); Sodium starch glycolate (SSG, S.D. Fine-Chem Ltd., Mumbai, Maharashtra, India) and Croscarmellose sodium (CCS, S.D. Fine-Chem Ltd., Mumbai, Maharashtra, India) were purchased. Fumed silica (aerosil), magnesium stearate, lactose and starch (Research Lab Mumbai, Maharashtra, India) were purchased. All other chemicals used were of analytical grade.

**Methods**

**Drug-Excipient Compatibility Studies**

**GPZ Identification and Calibration Curve**

Pure drug (GPZ) solution was prepared and identification was done spectrophotometrically (Shimadzu Corporation, UV-1800, Japan) within scanning range of 200 to 400 nm. For preparation of calibration curve, stock solution of GPZ was diluted serially several times in hydrochloric acid buffer pH 1.2 *USP (United States Pharmacopoeia)*[3] and analysed spectrophotometrically at observed $\lambda_{max}$.

**Fourier Transform Infrared Spectroscopy Analysis (FTIR)**

Pure drug (GPZ) and tablets from all batches (G1 to G3) were subjected to FTIR analysis by KBr method using Jasco FTIR-4100 recording spectrometer for estimation of compatibility. FTIR analysis was done in scanning range of 400 to 4000 $cm^{-1}$ and at resolution of 1 $cm^{-1}$.

**Formulation of Tablets**

By using wet granulation technique a total of three granule batches (G1 to G3) containing GPZ were prepared (Table 1). All powder ingredients were first sieved through 180 microns mesh size to obtain in uniform size and mixed with distilled water (granulating liquid) to obtain wet mass. Subsequently, uniformly sized granules were prepared by passing the wet mass through 850 microns mesh size. The wet granules were then subjected for drying in hot air oven (Bio Technics India, Mumbai, Maharashtra, India) for a period of 1 hour at 60 °C. Dried granules with narrow size distribution were further obtained by screening 600 microns mesh size and then mixed with fumed silica (glidant) and magnesium stearate (lubricant).

**Table-1: Formulation composition of GPZ tablets[a].**

| Name of Ingredient | G1 | G2 | G3 |
|---|---|---|---|
| GPZ | 10 | 10 | 10 |
| SSG | 300 | - | - |
| CCS | - | 300 | - |

| | | | |
|---|---|---|---|
| CPVP | - | - | 300 |
| Fumed silica (aerosil) | 13 | 13 | 13 |
| Magnesium Stearate | 25 | 25 | 25 |
| Lactose | 17 | 17 | 17 |
| Starch | 35 | 35 | 35 |
| Tablet total weight | 400 ± 5 | 400 ± 5 | 400 ± 5 |

[a.] All quantities are expressed in mg.

Tablets with constant hardness (4 - 5 Kg/cm$^2$) were prepared by compressing the dried granules (400±5 mg) using 8-station rotary tablet press machine (CIP Machineries Pvt. Ltd., Ahmedabad, Gujrat, India) having a set of 10-mm round flat-faced punch and die. Prepared tablets were subjected to hardening and elastic recovery effect by relaxing for 24 hours at ambient conditions[4]. After relaxation period, the tablets were characterized for different post-compression evaluation parameters such as hardness, friability, thickness, diameter, drug content, uniformity of weight including *in vitro* disintegration time (DT).

**Evaluation of GPZ Tablets**

**Weight Uniformity**

For uniformity of weight a sample of total 20 tablets was selected on random basis from each batch (G1 to G3) and individually weighed using electronic balance (Shimadzu AUX220). Individual tablet weight was compared with average weight for determination of % deviation. The tablet formulations complies uniformity of weight test if not more than two of the individual tablet weights deviate from the average weight by more than ± 5% (for 250 mg or more) as per pharmacopoeial standards[5,6].

**GPZ Content**

A pre-weighed sample of not more than 10 tablets from each batch (G1 to G3) was selected for determination of GPZ content and subsequently powdered using glass mortar and pestle. A weight of powder equivalent to 10 mg of GPZ was dissolved in 100 mL of hydrochloric acid buffer pH 1.2 *USP*[7,8]. From this solution suitable dilutions were

made and the resulting solution was filtered and analysed by UV-Visible spectrophotometer (Shimadzu Corporation, UV-1800, Japan) at 276 nm using hydrochloric acid buffer pH 1.2 *USP* as a reference. Further GPZ content of tablets was calculated with help of calibration curve. GPZ content in tablets was determined in triplicate (n = 3) for each batch (G1 to G3).

**Hardness**

All batches (G1 to G3) were subjected to evaluation of hardness for minimum of 3 tablets (n = 3) from every batch using a Monsanto-type hardness tester (Lab Hosp Corporation, Mumbai, Maharashtra, India). The tablet was held diametrically between the mobile and fixed surface and the indicator scale of tester was adjusted to zero reading. The force ($Kg/cm^2$) was applied gradually until tablet breaks and recorded as tablet hardness.

**Friability**

All batches (G1 to G3) were processed for determination of tablet friability by using Roche friabilator (Electrolab, Mumbai, Maharashtra, India) in triplicate (n = 3). A pre-weighed sample size of 10 tablets selected randomly was transferred in plastic chamber of friabilator. The chamber was allowed to revolve at 25 rpm for 4 min (100 revolutions) where a collective effect of abrasion and shock occurred due to tablet drop from 6 inches height in every revolution *(USP)*[9]. Then tablets were removed, dedusted and again weighed for determination of percentage friability (F) using equation 1. The tablet passes the friability test if observed % deviation (weight loss) for 10 tablets is not more than 1% *(USP)*[9].

$$F = \frac{W_0 - W_1}{W_0} \times 100 \qquad \text{..... 1}$$

Where, $W_0$ and $W_1$ indicate the weight of tablets before and after the test.

**Uniformity in Diameter and Thickness of Tablet**

Not more than 3 tablets were selected randomly from each batch (G1 to G3) for determination of uniformity in diameter and thickness. By using digital vernier calliper a crown-to-crown diameter and thickness of each tablet at 3 different locations was recorded. The allowed deviations for tablet dimensions are ± 5% of the tablet size.

**In vitro DT**

A sample size of randomly selected 6 tablets from each batch (G1 to G3) was processed in triplicate (n = 3) for estimation of *in vitro* DT by placing one tablet and adding disk in each tube of disintegration tester *USP* (Electrolab, ED-2L, Mumbai, Maharashtra, India). Distilled water (900 ml) maintained at 37 ± 2ºC was used as

immersion fluid. The time (seconds) at which the tablet gets completely disintegrated with no any sign of presence of palpable mass in tube was noted down as DT[10].

**Statistical Model Development**

Molecular structures of all polymers were drawn and minimized for energy content by Vlife Molecular Design Suite (MDS) 4.2. More than 115 molecular descriptors (more than 115) for each structure of polymer were calculated representing the physicochemical properties of polymers. The calculated descriptors were correlated with formulation characteristics of GPZ tablets and a set of descriptors (more than 50 descriptors) showing good correlation with characteristics was selected for further processing of data. Subsequently, training set molecules with known value of dependent variable were randomly selected and processed by random data selection method to yield several mathematical models. Moreover, the generated models have been tested for predictive ability using set of test molecules (not included in process of model development). Consequently, based on best correlation and significant effect on tablet characteristics, several descriptors were selected to obtain multiple sets (a single set with maximum of 5 descriptors). Further, obtained sets were processed as independent variables against tablet property under study (dependent variable) using multiple linear regression (MLR) technique by user defined variable selection method. This resulted into generation of several (minimum of 4) models. From these 4 models, a model with high coefficient of correlation and lower standard error was selected for each characteristic of tablet to elucidate the effect of polymer properties (Table 2) on response variable (DT, friability and hardness). Therefore, statistical modelling of tablet characteristics based on properties of polymer could help in selection of most correct polymer or polymer composite for required qualities as well as in deciding the composition of formulation in advance.

**Table-2: Set of polymeric descriptors in statistical model development.**

| Sr. No. | Name of descriptor | Description |
|---|---|---|
| 1. | H-AcceptorCount | Number of hydrogen bond acceptor atoms |
| 2. | H-DonorCount | Number of hydrogen bond donor atoms |
| 3. | XAHydrophobic Area | vdW surface descriptor showing hydrophobic surface area. (By |

| | | |
|---|---|---|
| | | Audry Method using Xlogp) |
| 4. | SAMostHydrophobic HydrophilicDistance | Signifies distance between most hydrophobic and hydrophilic point on the vdW surface. (By Audry Method using Slogp) |
| 5. | vdWSurfaceArea | Signifies total van der Waals surface area of the molecule. |

**Results and Discussion**

In present study, immediate release tablets of GPZ (from alkaline or basic class) were prepared using three different polymers and evaluated for several physical parameters. The physicochemical properties of polymers were calculated and subsequently used to build a statistical relationship with tablet evaluation parameters (*in vitro* DT, hardness and friability). As a consequence, the generated mathematical models could assist in deciding polymer system in advance and also the composition of formulation for required characteristics.

**Drug-Excipient Compatibility Studies**

**GPZ Identification and Calibration Curve**

Identification of GPZ was done by observing $\lambda_{max}$ at 276 nm in hydrochloric acid buffer pH 1.2 *USP* in agreement with previously reported results[11]. Calibration curve of GPZ at observed $\lambda_{max}$ showed slope, intercept and coefficient of correlation ($r^2$) at 0.00145, +0.001 and 0.9958, respectively in buffer pH 1.2.

**FTIR Analysis**

Identification of pure GPZ was also completed by recording characteristics peaks in FTIR spectra (Figure 1). Characteristic peaks for GPZ have been observed at 1031.84 for C-N, 1333 and 1159 $cm^{-1}$ for $SO_2NH$, 1431.26 for aromatic C-H bending, 1527.91 for C=C stretching, 1651.42 for C=O from urea group, 1689.11 for C=O from amide group, 3257.18 for aromatic C-H stretching and 3373.30 for N-H stretching. All these peaks were in agreement with reported standard peaks that confirms the molecule as N-[2-[4-[[[(Cyclohexylamino) carbonyl]amino]sulfonyl]phenyl]ethyl]-5–methylpyrazinecarboxamide or glipizide[12-14].

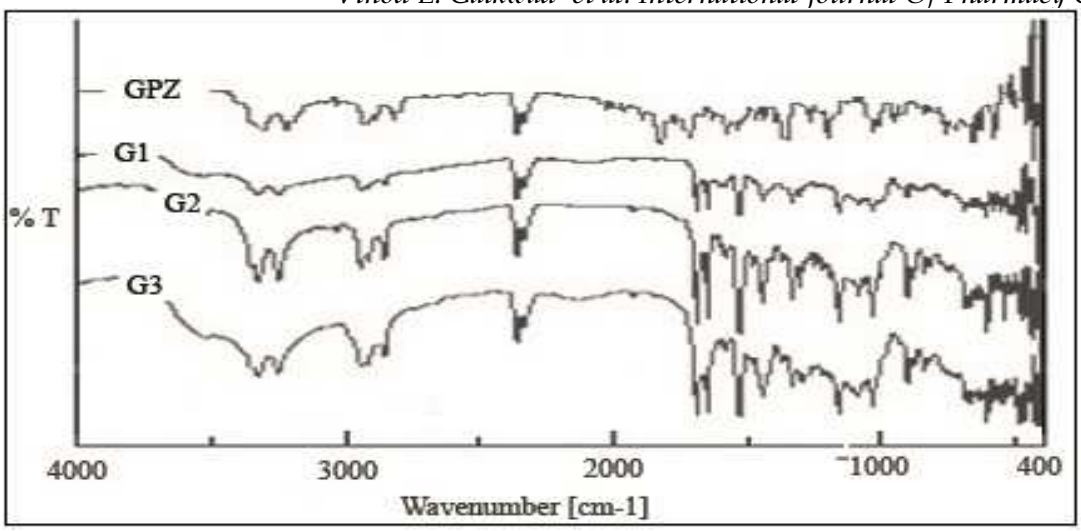


**Figure-1: FTIR Spectra for Pure drug (GPZ) and all Tablet Formulations (G1 to G3).**

FTIR spectra for tablets from all batches (G1 to G3) showed retention of GPZ peaks with very slight or negligible shifting of peaks (Figure 1) attributed to polymer adsorption on to the surface of drug indicating no interaction between GPZ and excipients used in formulation. Therefore, GPZ can be successfully formulated into tablets using selected excipients with retention of its potency.

**Evaluation of GPZ Tablets**

Tablets from all batches were observed without any defects and change in odour and colour, free from capping and sticking problem, showed smooth surface with flat shape. Subsequent to visual inspection, all tablet formulations were subjected for evaluation of several post-compression parameters.

**Weight Uniformity**

All batches (G1 to G3) have exhibited uniformity in weight as indicated by very slight % deviation (0.32 ± 0.42 to 0.55 ± 0.29) from average weight of tablet (Table 3) complying with stated official limits (± 5% deviation allowed for 250 mg or more average weight)[5]. This was attributed to formation of granules with good flowability that assures uniform die filling and compression of granules into tablets with constant weight and hardness.

**Table-3: Post-compression evaluation of GPZ tablet formulations[a].**

| Parameter | G1 | G2 | G3 |
|---|---|---|---|
| Weight Uniformity (% deviation) | 0.32 ± 0.42 | 0.55 ± 0.29 | 0.48 ± 0.37 |

| | | | |
|---|---|---|---|
| GPZ Content[#] (%) | 99.25 ± 1.87 | 101.34 ± 2.56 | 98.97 ± 2.35 |
| Hardness[#] (Kg/cm$^2$) | 4.32 ± 0.22 | 4.18 ± 0.13 | 4.01 ± 0.25 |
| Friability[#] (%) | 0.277 ± 0.025 | 0.550 ± 0.115 | 0.803 ± 0.050 |
| Thickness[#] (mm) | 4.13 ± 0.011 | 4.15 ± 0.035 | 4.12 ± 0.021 |
| Diameter[#] (mm) | 10.06 ± 0.007 | 10.07 ± 0.010 | 10.06 ± 0.005 |
| *In vitro* Disintegration Time[#] (sec) | 71.33 ± 8.02 | 53.33 ± 8.02 | 28.00 ± 5.00 |

[a.] All values are given as Average ± SD at n = 3[#].

**GPZ Content**

All tablet formulations (G1 to G3) have indicated uniform GPZ content ranging between 98.97 ± 2.35 and 101.34 ± 2.56 % (Table 3) within the prescribed official standards stating that glipizide tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of glipizide ($C_{21}H_{27}N_5O_4S$)[15].

**Hardness**

From Table 3, the hardness (4.01 ± 0.25 to 4.32 ± 0.22 Kg/cm$^2$) observed for tablets from all batches (G1 to G3) showed desirable strength of tablets against mechanical vibrations commonly experienced during machine handling and shipping. Hardness of tablets from all batches was found to be in good agreement with friability and *in vitro* DT results. Tablet with higher hardness is indicative of improved densification associated with decreased porosity that increases the time required for disintegration of tablet.

**Friability**

All tablet formulations passes the friability test as observed friability (0.277 ± 0.025 and 0.803 ± 0.050 %, Table 3) was found to be within the stated pharmacopeial standards (not more than 1%)[9]. Batch G1 showed lowest friability with high hardness indicating good strength and improved handling qualities as well as resistance against the mechanical shocks.

**Uniformity in Diameter and Thickness of Tablet**

From Table 3, uniformity in diameter (10.06 ± 0.005 to 10.07 ± 0.010) and thickness (4.12 ± 0.021 to 4.15 ± 0.035) for tablets from all batches (G1 to G3) has been observed as values were within the acceptable standards (± 5%) of the size of the tablet.

**In vitro DT**

Disintegration of tablets is performed to assure the complete accessibility of drug to medium for dissolution and its further absorption through various physiological barriers or membranes. Faster disintegration of tablet is commonly associated with the higher rate of diffusion of water molecules inside the tablet core attributed to the presence of disintegrant with high water uptake ability.

In present study, all batches indicated faster disintegration of tablets (within 72 sec). Batch G3 showed very shorter time (28.00 ± 5.00 sec) for disintegration containing CPVP as superdisintegrant. This was attributed to highly crosslinked structure of CPVP that lead to formation of interconnected capillary structure allowing higher water uptake and holding capacity without formation of gel. Commonly, CPVP followed wicking as the main mechanism for tablet disintegration. However, batch G1 (SSG) showed highest time (71.33 ± 8.02 sec) for disintegration of tablet. This was related to the lower wettability and hence water uptake capacity compared to CPVP and CCS. Batch G2 containing CCS indicated faster disintegration (53.33 ± 8.02 sec) than batch G1 due to high wetting capacity than SSG. Additionally, CCS showed swelling as the main mechanism for tablet disintegration.

Furthermore, formulations containing CCS and SSG formed fine and coarse size primary particles, respectively after disintegration of tablets. Therefore, disintegration mediated difference in particle size need to be highly considered for improving further dissolution and bioavailability of drug.

**Statistical Model Development**

Vlife MDS 4.2 commercial software was used to draw and energy minimize the molecular structures of polymers used in present study. Over 115 molecular descriptors have been calculated and subjected for building correlation with formulation characteristics of GPZ tablets (TD, friability and hardness). This leads to development of statistical models with an ability to elucidate the effect of physicochemical properties of polymers on tablet characteristics. The regression analysis data obtained from statistical modeling of GPZ tablet formulation is presented in Table 4.

**Table-4: Regression data of statistical models developed for GPZ tablets[a].**

| Sr. No. | Parameter | Coefficients of Regression Analysis | | |
|---|---|---|---|---|
| | | **Hardness** | **Friability** | **Disintegration Time** |
| 1. | $r^2$ | +0.9450 | +0.9657 | +0.9292 |
| 2. | F - test | 10.3098 (Analysis is significant) | 16.8768 (Analysis is significant) | 7.8687 (Analysis is significant) |
| 3. | Standard error | ±0.0856 | ±0.0717 | ±8.6263 |
| 4. | Intercept (Mean response) | +2.853 | +1.526 | -8.522 |
| 5. | H-AcceptorCount | -0.205 | -0.008 | -6.721 |
| 6. | H-DonorCount | +0.078 | +0.094 | +4.462 |
| 7. | XAHydrophobicArea | +0.001 | +0.038 | +0.020 |
| 8. | SAMostHydrophobic HydrophilicDistance | +0.005 | +0.002 | +2.280 |
| 9. | vdWSurfaceArea | +0.004 | -0.003 | -0.170 |

[a.] where $r^2$ and $q^2$ are observed and predicted correlation coefficients.

Different statistical models obtained for individual physical characteristic of tablet formulation were described as follows:

**Hardness**

$$Hardness = -0.205 \times H\_AcceptorCount + 0.078 \times H\_DonorCount + 0.001 \times XAHydrophobicArea + 0.005 \times SAMostHydrophobicHydrophilicDistance + 0.004 \times vdWSurfaceArea + 2.853 \ (\pm 0.0856) \quad \ldots 2$$

From statistical model developed for hardness (equation 2), a good correlation ($r^2$ = +0.9450) between all polymeric properties and GPZ tablet hardness with lower standard error (±0.0856) and intercept as +2.853 has been observed

(Table 4). This specifies that 94.50 % of the change in hardness of GPZ tablet can be elucidated by the change in the 5 polymeric descriptors. From F-test (10.3098) significant analysis was observed indicating significant impact of all descriptors on hardness. Hence, the developed model (equation 2) is able to quantitatively predictive the hardness of GPZ tablets based on study of polymeric descriptors or properties. 'H-AcceptorCount' showed a highest negative impact on hardness (regression coefficient = -0.205, Table 4) indicating reduction in hardness of tablet by inclusion of polymer with high hydrogen bond accepting capability. 'H-AcceptorCount' descriptor denotes the number of hydrogen bond acceptor atoms in the polymer structure. Conversely, 'H-DonorCount' showed a highest positive impact on hardness (regression coefficient = +0.078, Table 4) that denotes improved hardness of tablet in presence of polymer with high hydrogen bond donating capacity. 'H-DonorCount' descriptor signifies the number of hydrogen bond donor atoms in the polymer structure. Such increase in hardness or strength of tablet can be related to the higher hydrogen bonding between drug and polymer with higher 'H-DonorCount'. In present study, the regression coefficients verified the logical inverse relation between 'H-AcceptorCount' (-0.205) and 'H-DonorCount' (+0.078). Moreover, 'XAHydrophobicArea' showed a lowest positive impact on tablet hardness (regression coefficient = +0.001, Table 4). 'XAHydrophobicArea' is a vdW surface descriptor that shows hydrophobic surface area (by Audry method using Xlogp). This indicated very slight improvement in hardness of tablet in presence of polymer having high 'XAHydrophobicArea'. Similarly, 'SAMostHydrophobicHydrophilicDistance' showed a positive effect on tablet hardness (regression coefficient = +0.005, Table 4). 'SAMostHydrophobicHydrophilicDistance' descriptor specifies the distance between most hydrophobic and hydrophilic point on the vdW surface (by Audry method using Slogp) and hence polarity on molecule surface. Therefore, an increase in strength and hardness was observed with inclusion of polymer having increased distance or reduced polarity. Additionally, 'vdWSurfaceArea' also indicated positive correlation with tablet hardness (regression coefficient = +0.004) as given in Table 4. 'vdWSurfaceArea' descriptor signifies total van der Waals surface area of the molecule. Therefore, increase in surface area is associated with increased physical bonding sites between particles with net result of improved hardness of tablet.

**Friability**

$$Friability = -0.008 \times H\_AcceptorCount + 0.094 \times H\_DonorCount + 0.038 \times XAHydrophobicArea + 0.002 \times SAMostHydrophobicHydrophilicDistance - 0.003 \times vdWSurfaceArea + 1.526 \ (\pm 0.0717) \quad \ldots 3$$

Equation 3 denotes a mathematical model that indicates a good statistical relationship between all polymeric

properties and friability ($r^2$ = +0.9657) with minimum standard error (±0.0717) and intercept as +1.526 (Table 4). From F-test (16.8768) a significant analysis has been observed. It has been observed that a change in the 5 descriptors is able to detect the 96.57 % of the change in friability and hence, tablet friability can be predicted significantly on basis of calculated polymeric descriptors. From regression coefficient (-0.008, Table 4) a slight negative impact of 'H-AcceptorCount' on friability has been observed that indicates a small reduction in tablet friability in presence of polymer having considerable hydrogen bond accepting ability. However, 'H-DonorCount' showed surprising positive results of regression analysis for both hardness and friability. 'H-DonorCount' compared to 'H-AcceptorCount' indicated an equal and opposite effect on friability as indicated by highest positive regression coefficient (+0.094, Table 4). This represents the reduction in friability with inclusion of polymer having lower hydrogen bond donating ability. Therefore, polymer having lower H-bond donor ability or higher H-bond acceptor ability found to accept the H-bond from drug molecule that lead to formation of tablet with greater hardness or strength. 'XAHydrophobicArea' also showed a positive impact on friability (regression coefficient = +0.038, Table 4) indicating a significant increase in friability of tablet by polymer having high 'XAHydrophobicArea'. From Table 4, regression coefficient (+0.002) showed a similar but very minute impact of 'SAMostHydrophobicHydrophilicDistance' on friability of tablet. This was attributed to the reduced net polarity on polymer surface with relative increase in its surface hydrophobicity, which is in accordance with results observed for 'XAHydrophobicArea'. Conversely, 'vdWSurfaceArea' represented a negative impact on friability (regression coefficient = -0.003, Table 4) which is in good agreement with equal and opposite regression result observed for hardness. Increase in surface area found to facilitate the physical bonding between particles of polymer and other ingredients with further reduction in friability of tablets.

**DT**

$$DT = -6.721 \times H\_AcceptorCount + 4.462 \times H\_DonorCount - 0.020 \times XAHydrophobicArea - 2.280 \times SAMostHydrophobicHydrophilicDistance + 0.170 \times vdWSurfaceArea - 8.522 \ (\pm 8.6263) \quad \ldots 4$$

A regression coefficient (+0.9292) of model generated for DT (equation 4) showed a good statistical relationship between 5 properties and DT, indicating a change of 92.92% in DT can be elucidated by a change in 5 independent variables. The model showed significant analysis (F-test = 7.8687) with low standard error (±8.6263) and overall mean response as -8.522 (Table 4) and hence, the developed model can be used to study the effect of individual property on DT of GPZ tablets. 'H-AcceptorCount' showed a highest negative impact on DT (regression coefficient

= -6.721, Table 4) specifying the faster disintegration of tablet with inclusion of polymer having high hydrogen bond accepting capability. The polymer formed hydrogen bonds easily with high number of water molecules than drug where both are competing simultaneously for H-bonding sites on polymer. This resulted into faster water uptake by polymer and faster disintegration of tablet. Conversely, a highest positive effect of 'H-DonorCount' on DT (regression coefficient = +4.462, Table 4) has been observed which is in good agreement with common inverse relation that exist between 'H-AcceptorCount' and 'H-DonorCount'. The positive effect indicated the increase in DT in presence of polymer having high 'H-DonorCount'. The regression coefficients observed for both 'XAHydrophobicArea' (-0.020) and 'SAMostHydrophobicHydrophilicDistance' (-2.280) have shown a considerable positive effect on DT (Table 4). Both these descriptors are indicative of reduced polarity on polymer surface that gives slower disintegration of tablets attributed to reduced wetting in presence of polymer having higher hydrophobic area. However, increase in polymer surface area associated with high and quick uptake of water molecules resulted into faster disintegration of tablet as indicated by negative effect (regression coefficient = -0.170, Table 4) of 'vdWSurfaceArea' on DT.

Therefore, tablet formulations with desired physical characteristics can be successfully prepared by selecting a polymer system majorly based on its hydrogen acceptor and donor count. Also, such modeling of physical attributes based on polymeric properties could assist in prediction of composition of formulation for desired characteristics.

**Conclusion**

The developed mathematical models in present research can be successfully used to quantitatively predict the physical characteristics of tablets such as hardness, friability and disintegration time on basis of estimated polymeric properties. Additionally, the models could have an ability to predict the characteristics of formulation containing polymers that resemble in physicochemical class with polymers used in present study. Hence, statistical modeling would help to decide the formulation composition in advance with saving of time and cost of industry.

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