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BAPA

BANGLADESHI-AMERICAN PHARMACISTS' ASSOCIATION

INSIGHT OF A COUNSELING PHARMACIST

- SIMULTANEOUS ASSAY OF BACLOFEN, LIDOCAINE, AND KETAMINE IN COMPOUNDED TOPICAL CREAM
- CARDIOVASCULAR DISEASE RISK FACTORS IN SOUTH ASIANS: A LITERATURE REVIEW
- DEVELOPMENT AND EVALUATION OF WATER DISPERSIBLE TABLETS OF ACYCLOVIR

AN ANNUAL PUBLICATION FROM THE EXECUTIVE COMMITTEE, BAPA

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PHARMACISTS' ASSOCIATION

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- Quamrun Masuda, Mamoon Rashid, Nasheed Shams and Randy Mullins
- Margaret Tsopanarias
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LEETU MOHAMMED ZAMAN

Departed Souls

We deeply regret and mourn the departure of our fellow friends.
We miss them a lot and remember them in our prayers.
In this day of the Convention we will miss their presence.

Abdullah Al Sad
Abu M Kabir
Abdul Mannan Khan
Dr. Faisal
Muhammad Enamul Malik
Kamrul Khan
Md. Lutful Haque
Mohammad Rafiqul Islam(Benu)
Manju Biswas
Mohammad Azim
Mohammad Sikandar
Mohammed Fazli Hussain
Mohammed Wahidur Rahman
Muzammel Khan
Nazir Ahmed
Qamrul Huda Fiaz
Dr. Rashid
Sujash Chandra Guha Roy
Utpal Kanti Biswas

Disclaimer: If we missed anybody's name it is an unintentional mistake.

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BANGLADESHI – AMERICAN PHARMACISTS' ASSOCIATION

26th Annual Convention Programs

AUGUST 18TH - AUGUST 20TH

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BAPA CONVENTION SCHEDULE AT-A-GLANCE

Day 1	**Friday, August 18th, 2017**
12:00 PM	Registration
6:00 PM - 8:00 PM **SALON B**	*Continuing Education*: **Medication Therapy Management (MTM)** *Dr. Eusra Shams, PharmD.*
8:00 PM - 10:00 PM **BAYVIEW BALLROOM**	Dinner and Cultural Program

Day 2	**Saturday, August 19th, 2017**
7:00 AM - 9:00 AM **MAIN DINING ROOM**	Breakfast
9:00 AM - 12:00 PM **SALON B**	*Continuing Education:* **Medication Adherence: Point of Care Interventions** *Presenter: Dr. Quamrun Masuda, PhD., RPh.* *Associate Professor, VCU School of Pharmacy*
10:00 AM - 11:00 PM **Cape May**	Yoga for women only (Session 1)
11:00 AM - 12:00 PM **Cape May**	Yoga for women only (Session 2)
11:00 AM - 5:00 PM **Reeds Bay**	Henna and Mendhi by Raeqa Nuha Mahmud (Women only)
11:00 AM - 11:00 PM	Sari and Jewelry vendors (Harding and Eisenhower Room)
11:00 AM - 5:00 PM	Pharmacy Trade show
12:00 PM - 1:00 PM **SALON B**	*Continuing Education:* **Drug Regulatory Process Overview- A US Perspective** *Presenter: Naushad Islam, M.S.* *Senior Director and Global Regulatory leader at Johnson and Johnson Pharmaceuticals*
1:30 PM - 2:30 PM **BAYVIEW BALLROOM**	Lunch

3:00 PM - 4:00 PM **SALON B**	*Continuing Education:* **Issues in Women's Health** *Presenter: Dr. Maleka Z Ahmed, MD. Assistant Professor, Duke University Medical Center* *(Joint session with pharmacists and non-pharmacists)*
4:00 PM - 5:00 PM **SALON B**	*Continuing Education:* **Cultural Competence in Pharmacy** *Presenter: Dr. Charnicia Huggins, PharmD., MS, BCACP, Clinical Pharmacist at Bronx Lebanon Hospital Center* *(Joint session with Pharmacists and non- pharmacists)*
7:30 PM - 12:00 AM **BAYVIEW BALLROOM**	**Dinner and Cultural program**

Day 3	**Sunday, August 20th, 2017**
8:00 AM - 10:00 AM **MAIN DINING ROOM**	**Breakfast**
10:00 AM - 12:00 PM **SALON B**	*Continuing Education:* **Care Transitions: The Pharmacist's Role in Preventing Medication Errors** *Presenter: Dr. Charnicia Huggins, PharmD., MS, BCACP, Clinical Pharmacist at Bronx Lebanon Hospital Center*
12:00 PM	**Check Out**

For further update or changes, please visit our website at http://www.bapainfo.org

Message from the PRESIDENT

Mohammed
SHABBIR TAHER

Dear members of the Bangladeshi-American Pharmacists Association, guests, friends and family,We are truly honored to have your presence here tonight for our 26th annual convention.

Most of you know last year we celebrated our 25th anniversary; we had well over 250 members and guests in attendance. We had a chance to embrace and relive the memory of BAPA since its inauguration. Following the dinner we held another successful convention in September. So I thank all the members, vendors and sponsor for participating in our events.

We set a goal to increase our membership not just here in the Tri- State area but all over the country, There are over many pharmacist's with Bangladeshi origin are practicing in the state of Florida , And most you know by now BAPA held its first regional meeting in state of Florida on April 8th, 2017. We thank everyone who participated in that event.

Last but not least we have to make sure we take time to prepare future pharmacist. We have to constantly learning while we practice and pass down that knowledge to the next generation.

May God bless BAPA, may God bless the profession of pharmacy, and may God bless this great country of the United States.

Thank you.

Mohammed Shabbir Taher, R.Ph., Pharm.D
President, BAPA

Message from the VICE PRESIDENT

Fahim
AHMAD

Thank you for allowing me the privilege of serving as your vice president. I see great things ahead for the future of BAPA. We have successfully used technology to generate revenue and streamline operations to make things easier for our members. I hope to be involved in this continued process.

Thank you for your attendance at this years annual convention. We hope you all have a wonderful time!

Fahim Ahmad
Vice President, BAPA

Message from the GENERAL SECRETARY

Nishad
HOQUE

Thank you for giving me the opportunity to serve as BAPA Secretary for the second straight year. It is the time of the year when all BAPA members meet and greet take place with pleasant and wonderful atmosphere everywhere. I along with the President and Vice President welcome all our fellow members of BAPA in this 2017 convention.

This is an exciting time for BAPA as the convention is always a wonderful opportunity to meet new people in different areas of pharmacy grounds like industry, hospital, health care and retail. Eating all halal food, enjoying the cultural show and earning Continuing education credits and relaxing for three days from our busy schedules.

I look forward to welcome all new comer and new pharmacists their family members. At the end best of luck for this year convention and current committee who is working hard day and night to make this even successful. May Allah bless all of us!

Thank you

Nishad Hoque , Pharm D, R.Ph
Secretary, BAPA

Message from the TREASURER

Fariha
KABIR

I am honored to be part of the Executive Board and to serve as the Treasurer of BAPA for the first time. This organization has been a integral part of my family life since its inception and I would like to thank the entire BAPA community for being a positive influence in my upbringing. As the daughter of the late past President, Abu M. Kabir, I take great pride in expanding his legacy and devotion to BAPA. I have always been impressed with the numerous accomplishments of our organization and our dedicated leadership among the pharmacy community around the world over the years. I am particularly motivated to work on supporting our efforts for continued funding of student scholarships and awards as well as providing funds for further research on groups.

As an active practicing pharmacist for four years, I have thoroughly enjoyed the opportunity to join with colleagues who have become family in efforts and activities to spread awareness of BAPA's mission. I am excited to be directly involved in the development of our organization and am positive that the future of BAPA will only flourish. As treasurer, I have worked in collaboration to recruit the largest number of new members in BAPA history and hope to grow the organization further. My goal is to work closely with the new generation of pharmacists to raise funds and establish relations with other healthcare professionals to bring BAPA to the forefront of professional pharmacist organizations.

On behalf of the rest of the Executive Board, I would like to show our appreciation to our President and Vice President for continuously working to evolve BAPA into a stronger organization by bringing innovative ideas while maintaining BAPA's core values.

Fariha Kabir, Pharm.D, R.Ph
Treasurer, BAPA

Articles

Articles

BAOJ Pharmaceutical Sciences

Quamrun Masuda, et al, BAOJ Pharm Sci 2017, 3: 2
3: 036

Research

Simultaneous Assay of Baclofen, Lidocaine, and Ketamine in Compounded Topical Cream

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Abstract

This study was conducted to determine the potency of the compounded topical preparation CPRM1 in Lipoderm base. CPRM1 is a coded proprietary formula developed by the Professional Compounding Centers of America and historically compounded and dispensed by Cavalier Pharmacy, located in Wise, Virginia. CPRM1 is compounded in response to prescriptions for chronic-pain management from local physicians for local patients. The research laboratory of Appalachian College of Pharmacy, located in Oakwood, Virginia, performed an assay of CPRM1 cream, using gradient reversed-phase high-performance liquid chromatographic method. This cream contained Baclofen, Lidocaine, and Ketamine. The assay results of all three drugs in the preparation were within ±10% of the labeled strength and ensured quality per guidelines in *United States Pharmacopeia* (USP) Chapter <795>Pharmaceutical Compounding–Nonsterile Preparations [1]. The investigators developed a simple and reproducible gradient high-performance liquid chromatographic assay method, and performed abbreviated validation to establish the specificity, recovery, accuracy, and precision of the method for quantitative analysis of three active pharmaceutical ingredients-baclofen, lidocaine, and ketamine-in the preparation. The compounded cream, CPRM1, was analyzed in quadruplicate.All three drugs were found to be within the limit of acceptance as set forth in the *United States Pharmacopeia* Chapter <795>. The chromatographic condition of this simultaneous analysis was simple. The elution solvent contained 12% acetonitrile and 88% phosphate buffer with pH adjusted to 3.6. All three drugs were eluted as sharp, symmetrical peaks, with the elution being completed within 15 minutes. The isocratic elution mode, after elution of the last focused compound, was changed to gradient mode to wash out the residuals, and the run was completed in 30 minutes. CPRM1 was stored at room temperature to verify stability of these three drugs in the compounded cream. The study continued for 12 weeks (i.e., approximately 3 months), with weekly sampling. Assay results of all three drugs demonstrated >90% of the label claim during the 12-week stability study period.

Introduction

A survey shows about 30.7% of adults in the U.S. suffer from pain that occurs from various origins [2]. Neuropathic pain is one of the most critical pain. This condition creates complex challenges for effected individuals because of its impact on quality of life, in addition to its treatment costs. Neuropathic pain refers to a painful disorder characterized by dysfunction or disease of the nervous system at a peripheral level, or central level, or both. Research shows neuropathic pain may result from any of the following causes, diabetic neuropathy, chemotherapy-induced neuropathy, postherpetic neuralgia, etc. [3]. Currently clinicians combine *N*-methyl-D-aspartate(NMDA) receptor blockers (for example, ketamine), glutamate and/or α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) antagonists (for example gabapentin, carbamazepine, valproic acid, or phenytoin), gamma-aminobutyric acid (GABA) agonist (e.g., baclofen), and other receptor agonists or antagonists for treatment [4]. Commercial products of these drugs are mostly in oral-dosage form, which create a number of adverse effects.

Contemporary trends for chronic pain management also include personalized compounded topical preparations [5,6]. These preparations contain combinations of active pharmaceutical ingredients with the objective of providing synergistic effect in pain

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management. The *Globe Newswire* conducted a national survey in 2013, addressing the use of "Prescription Topical Creams" in chronic pain management. More than 83% of about 3,600 respondents reported a significant reduction in their pain after using custom compounded prescription pain creams [7]. The survey respondents reported that the creams reduced their pain levels by more than half, on average. More than 5% of respondents reported that the creams eliminated their pain. In addition, 38% reported reducing other oral-pain medications while using the creams. A placebo-controlled clinical trial concluded that transdermal cream containing ketamine and lidocaine was effective in 73% of patients with acute neuropathic pain and may be a good alternative to oral medications [8]. Topicalpain preparations currently approved in the U.S. are:

Diclofenac sodium 1.5% topical solution

Diclofenac sodium gel 1%

Diclofenac hydroxyethylpyrrolidine 1.3% patch

Each of these topical nonsteroidal anti-inflammatory drug (NSAID) products delivers drugs to subcutaneous tissues for the management of pain associated with osteoarthritis or soft-tissue injuries. Topical NSAID preparations approved in the European Union include ibuprofen creams and gels, ketoprofen gel, felbinac gel and cutaneous foam, and piroxicam gel. Meta-analyses have confirmed the efficacy and safety of these preparations [9]. The Professional Compounding Centers of America (PCCA) conducted a transdermal penetration study of lidocaine, ketamine, baclofen, and gabapentin that included their proprietary vehicle Lipoderm, using a Franz cell model and human skin as the penetration barrier. The study data demonstrated that all four drugs penetrated through the excised skin and reached their peak level at various time points, confirming the usefulness of Lipoderm as a vehicle for extemporaneous compounding [10].

Baclofen (Figure 1), molecular weight 213.7, is an agonist at the gamma-aminobutyric acid type B (GABAB)receptor. Studies have reported its efficacy in trigeminal neuralgia. It is often use in trials on any type of neuropathic pain. The effective dose range is very wide (20 mg/day to >200 mg/day orally) and titration from a low initial dose is necessary. Baclofen is a muscle relaxant that, when used topically, is effective in doses with minimal systemic absorption [11].

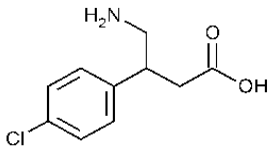

Figure 1: Structural formula of Baclofen.

Lidocaine (Figure 2) is a local anesthetic. It has a molecular weight of 234.34 and pK_a of 8.01. A 2004 study, published in *The Oncologist*, showed that a lidocaine transdermal patch provides analgesia in postherpetic neuralgia by reducing aberrant firing of sodium channels on damaged pain fibers located directly under the patch [12]. Amount of lidocaine absorbed from the patch is insufficient to cause systemic effects or local anesthesia. Other laboratory studies of compounded topical creams support their use for other neuropathic pain [13]. Topical lidocaine gel is also thought to reduce discharges of small afferent nerve fibers by blocking voltage-gated sodium channels [14].

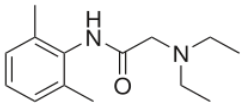

Figure 2: Structural formula of Lidocaine.

Ketamine (Figure 3) is an arylcyclohexylamine derivative, an NSAID. Its molecular weight is 237.7. A low dose of ketamine produces strong analgesia in neuropathic pain, most likely by inhibition of the NMDA receptor, although other mechanisms are possibly involved, including enhancement of descending inhibition and anti-inflammatory effects at central sites [15-17].

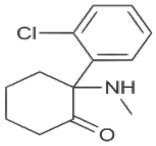

Figure 3: Structural formula of Ketamine.

The physicians these days often manage chronic pain of various origins, such as fibromyalgia, reflex sympathetic dystrophy, arthropathies, painful neuropathies, etc. using personalized topical compounded preparations, like gels, creams, and solutions of the above mentioned drugs. These preparations demonstrated site-specific treatment while decreasing or eliminating systemic side effects [18,19].

The CPRM1 cream is a compounded preparation, containing multiple drugs. This combination has been prescribed by local physicians to manage pain in diabetic neuropathy, postherpetic pain, and pain of complex origin. The purpose of this study was to determine the strength of baclofen, lidocaine, and ketamine, in this CPRM1 compounded preparation using HPLC method. Our study, conducted at the Appalachian College of Pharmacy, reports the strengths of lidocaine, ketamine, and baclofen in CPRM1 cream. This study also reports the stability of these three drugs in the preparation for a period of 12 weeks.

Materials and Methods

Chemicals, Reagents, and Equipment

The compounded preparation CPRM1 in Lipoderm cream was provided by Cavalier Pharmacy, Wise, Virginia.

Ketamine hydrochloride (HCl) USP (Lot 106286/E), and Baclofen USP (Lot 104470/E) were purchased from Medisca Inc. in Plattsburgh, New York. Lidocaine HCl monohydrate USP (Lot 1AL0451) was purchased from Spectrum Chemical Mfg. Corp. Chromatographic mobile phase modifier trifluoroacetic acid (Lot A14365-18), buffer salt monobasic potassium phosphate (Lot 90870),and polyether sulfone syringe filter, 25mm with a 0.4-µm pore size (Lot 12463112),were purchased from VWR International LLC in Radnor, Pennsylvania. Nitrocellulose filters with 0.45-µm pore size (Lot R2EA164961), and the vacuum pump Maxima Dry, Model PU1306-N820-9.01, were purchased from Fisher Scientific Company LLC, Hanover Park, Illinois.

Double-distilled water was prepared in-house using the all-glass Accumax India (Model AI-179) distiller. Methanol (Lot 51104) was purchased from EMD, Darmstadt, Germany, and HPLC-grade acetonitrile was purchased from VWR International.

Chromatographic Instrumentation

Waters Alliance 2695 Separation Module was used for the reverse-phase chromatography with Symmetry C-18, 5-µm (4.6×150mm) column. Analytes were detected and quantified using a Waters 2996 Photodiode Array (PDA) detector. Post-run analyses were performed at 220nm wavelength in the PDA. The separation system also had built-in degassing equipment. All chromatographic data were processed using Waters Empower 2 software, database version 6.10.00.00. The chromatographic separation assembly and the column were purchased from Waters Corporation, Milford, Massachusetts.

Mobile Phase and Sample Preparation

Preparation of Buffer

Stock buffer solution, 1M, was prepared by dissolving 68.04 g of monobasic potassium phosphate (molecular weight 136.09) in 500 mL of freshly prepared double-distilled water. The stock buffer was diluted to 25 mM with distilled water, and its pH was adjusted to 3.6 with 1M HCl. A few drops of trifluoroacetic acid were added to this buffer solution, as a solvent modifier. The buffer solution was filtered through a vacuum filtration unit, using a 0.4-µm filter. Acetonitrile and the freshly prepared buffer solution were mixed online at 12:88% v/v ratio for the isocratic elution part of the analyses. The solvent flow rate was maintained at 1 mL/min.

CPRM1 Samples and Standard Solution

Sample: Topical Cream CPRM1

About 500mg of the sample cream was transferred to a 10-mL glass beaker. About 5mL of acetonitrile was added to the beaker, and the cream was stirred with a glass rod. While the drugs were dissolved in acetonitrile, the insoluble cream matrix formed agglomerates. The supernatant liquid was transferred to a 50-mL volumetric flask and 5mL of fresh acetonitrile was added to the agglomerate, mixed briefly, and transferred carefully into the volumetric flask. The process was repeated again. One drop of 1M HCl was added to the flask in order to facilitate dissolution of baclofen. The flask was then sonicated for 5 minutes and set on cooling for about 10 minutes before adjusting the volume to 50mL. This formed the stock sample solution. The stock sample solution was filtered through a 0.45-µm syringe filter. Methanol, 10% v/v in water, was used as a diluent to prepare all working sample solutions. The stock filtrate was diluted to various extents to prepare a working sample solution, based on the concentration of the drug of interest.

Six milliliter (6 mL) of the filtrate was diluted to 100mL to determine the nominal concentration of ketamine; 2 mL of the stock filtrate was diluted to 10 mL to determine the concentration of lidocaine; and 5mL of the stock filtrate was diluted to 10mL to determine the concentration of baclofen. These final sample solutions were again filtered through syringe filters prior to filling the HPLC vials.

Preparation of the Stock Standard Solution of Drugs

USP referencestandards of ketamine, lidocaine, and baclofen, 25mg each, were accurately weighed and transferred into a 50-mL volumetric flask. The drugs were dissolved in 50% methanol in water, with intermittent sonication. One drop of 1M HCl was added to the solution to facilitate dissolution of the baclofen standard. This primary stock solution contained 500µg/mL of each of the standards.

Preparation of the Working Standard Solution of Drugs

The primary standard solution, 25mL, was transferred to a 100-mL flask and made up to the final volume with 10% methanol in water. This combined standard solution contained 125µg/mL of each of baclofen, lidocaine, and ketamine, and was used as 125% strength of the calibration curve. This strength of standard solution was diluted to prepare 100µg/mL, 75µg/mL, 50µg/mL, and 25µg/mL by diluting each of 8mL, 6 mL, 4 mL, and 2 mL to a final 10-mL volume with 10% methanol in water. These five concentrations were always used to develop the standard curve with freshly prepared stock and working standard solutions.

Results and Discussion

Method Development and Optimization

A sensitive RP-HPLC method has been developed for the simultaneous analysis of baclofen, lidocaine, and ketamine in a compounded CPRM1 preparation. The mobile phase of the method was composed of 12% acetonitrile and of 88% 25mM buffer (pH 3.6), with a few drops of solvent modifier TFA. At this composition, the peaks of baclofen, lidocaine, and ketamine were separated from the solvent front and from any other eluents. Since the cream contains a number of other ingredients, a gradual

gradient was used to wash out the residual chemicals from the column. Therefore, the mobile phase remained isocratic (12% acetonitrile and 88% buffer) for the first 15 minutes and then gradually increased acetonitrile concentration to 80% and buffer concentration was gradually decreased to 20%. After 25 minutes, the mobile phase composition was changed back to the original form (12% acetonitrile and 88% buffer). Hence the total run-time was set at 30 minutes.

The method was optimized with emphasis on specificity, linearity, accuracy, reproducibility, and adaptability for routine use in the laboratory.

Typical Chromatographic Profiles

Figure 4 shows the simultaneous separation of the three drug substances, baclofen, lidocaine, and ketamine, as these are combined in the reference standard solution and in the extracted solution of CPRM1 cream (Figure 5). All three peaks were sharp, symmetrical, and eluted with baseline resolution. Although peak responses are intense at 193 nm, we have chosen to use 220 nm to improve the signal-to-noise ratio. Under the established chromatographic condition, retention time of baclofen, lidocaine, and ketamine was 7.2, 10.2, and 11.8 minutes, respectively.

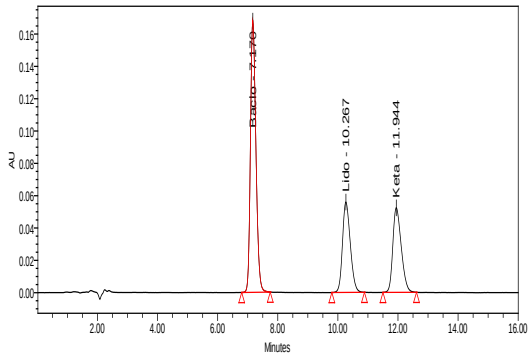

Figure 4: A typical chromatogram of baclofen, lidocaine, and ketamine in standard solution.

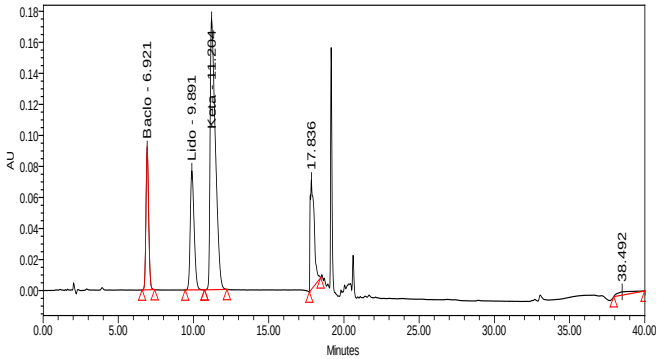

Figure 5: A typical chromatogram of baclofen, lidocaine, and ketamine in CPRM1 sample solution.

Specificity of the Method

The peak purity indices of all three drugs in standard and in sample solutions were determined with a PDA detector, under optimized chromatographic conditions. All three drugs demonstrated a smaller purity angle than the purity threshold (Figure 6), indicating that no additional peaks were co-eluted with any of these three drugs. Table 1 summarizes the results of specificity and peak purity.

Table 1. Specificity of the chromatographic method determined by Peak Purity Test during Simultaneous Analysis of Baclofen, Lidocaine, and Ketamine.

Component	Purity Angle	Purity Threshold	Comment
Baclofen	0.126	0.387	No co-elution
Lidocaine	0.190	0.441	
Ketamine	0.246	0.515	

Linearity and Range

The nominal expected concentration of the test solution for each of the three drugs was 100µg/mL. The calibration curves were constructed with five standard solutions, covering from 25% to 125% of the nominal concentrations, inclusive. The peak-responses of each of the three drugs were plotted against the corresponding drug concentrations in the linear regression analysis model. The correlation co-efficient of all three "line of best fit" are summarized in Table 2, together with the slope and the intercept of each line. The close approximation of the R^2 value to "1.0" (c.f. Table 2) demonstrates superimposition of the experimental values to the "Least Square Analysis" model. The linearity plots are in Figure 7.

Table 2. Calibration Data Showing Linearity of the High-performance Liquid Chromatographic Method for Simultaneous Analyses of Baclofen, Lidocaine, and Ketamine.

Concentration (mcg/mL)	Absorbance Unit at 220 nm		
	Baclofen	Lidocaine	Ketamine
25	854555	321808	354878
50	1734184	653298	719189
75	2605007	976416	1088915
100	3483853	1310750	1451755
125	4341482	1646469	1814570
R^2	0.99998	0.999907	0.999898
Intercept	-13240.7	-5232.19	1707.459
Slope	34894.1	0.379051	1.10431

Accuracy and Precision

The CPRM1 cream was extracted in four replicates. Strength of each of the three drugs baclofen, lidocaine, and ketamine, were determined in each replicate of sample. The assay results, together with the average strength, standard deviation, and the coefficient of variation (%RSD), are shown in Table 3. The percent relative

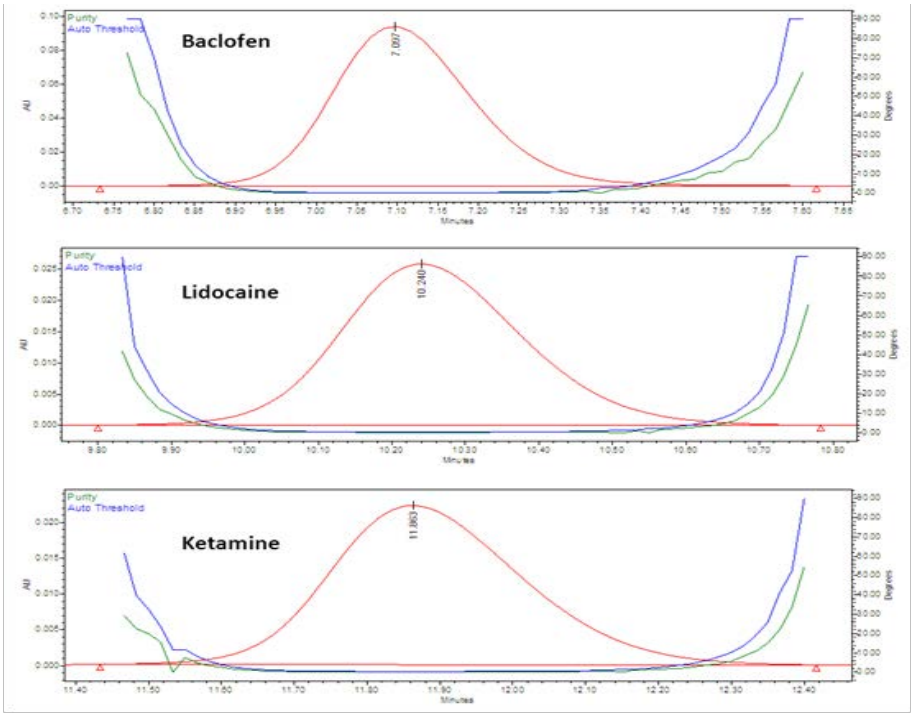

Figure 6: Peak purity (specificity) profile of baclofen, lidocaine, and ketamine in CPRM1 sample solution.

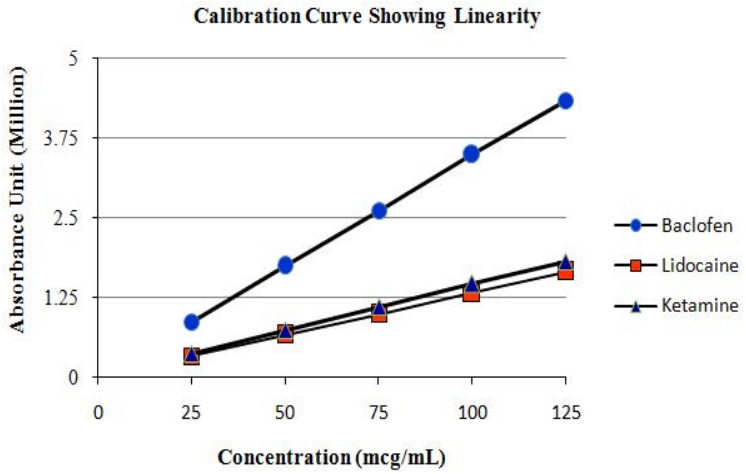

Figure 7: Calibration curves, demonstrating linearity of responses of baclofen, lidocaine, and ketamine.

standard deviations of the quadruplicate assay results are <2, indicating reproducibility and precision of the of the method and simultaneous analysis of CPRM1 topical cream.

Table 3. High-performance Liquid Chromatographic Assay of CPRM1 Cream in Replicate Analyses, Showing Accuracy and Precision of the Analytical Method.

Parameters	Recovery (% Label Claim) of Drugs		
	Baclofen	Lidocaine	Ketamine
CPRM1 Sample 1	100.87	98.91372	105.1
CPRM1 Sample 2	100.57	100.426	103.01
CPRM1 Sample 3	100.93	100.8135	105.03
CPRM1 Sample 4	100.82	99.57151	105.21
Average (n = 4)	100.80	99.93	104.59
Standard Deviation	0.158	0.854	1.054
%RSD	0.157	0.855	1.008

Assay of Ketamine, Baclofen, and Lidocaine

The investigators extracted freshly prepared CPRM1 cream, received from Cavalier Pharmacy, and determined the percent label claim of each of the three drugs in the sample. The recovery profiles are in Figure 8 at initial assay in the time-dependent assay profile. The recovery of all three drugs was within the limits of acceptance, defined by *USP* Chapter <795>.

Stability of Baclofen, Lidocaine,and Ketamine in CPRM1

The CPRM1 cream was stored at room temperature in the laboratory, with the inter- and intra-day excursion of the laboratory temperature 23°C±3°C. A sample of the CPRM1 cream was extracted to perform the stability study of the cream, every week for 12 weeks, with the exceptions of week 4 and week 6 due to unavailability of the HPLC equipment. The stability sample was analyzed for drug contents. All data were within the limits defined by the *USP*, confirming stability of all three drugs in CPRM1 cream. The assay profiles of each of these three drugs are shown in Figure 8.

Conclusion

Quality-control guidelines in compounding processes have progressed considerably in the recent past, since the first edition of the *USP*, with regulations in Chapter <795>. Personalized compounded preparations require skill, specialized training, and expertise. The re-emergence of compounding preparations as a personalized pharmacy service warrants close attention to the quality of the preparation and the service. The compounding pharmacist is responsible for making preparations of acceptable strength, quality, and purity, with appropriate packaging and labeling in accordance with *USP* guidelines. Most of the compounding pharmacies do not have the infrastructure to determine the "strength" and the "beyond-use date" of their compounded preparations. Many commercial resources are becoming available to the compounding pharmacist, from third-party quality-control testing laboratories to extensive training programs. Appalachian College of Pharmacy scientists provide quality verification, compounding preparation development, and regulatory services to the neighborhood and regional compounding pharmacies, not for profit, but as a part of "community pharmacy support services" program of the College.

The current analysis demonstrated that the compounded CPRM1 cream in Lipoderm complied with *USP* Chapter <795> regulations based on its drug strengths. Baclofen, lidocaine, and ketamine were stable over a 12-week (3-month) period. Amounts of ketamine, lidocaine, and baclofen were verified to be >90% of strengths stated on the preparation label. Since these are prescription-driven compounded preparations, we decided not to continue the stability studies longer than three months.

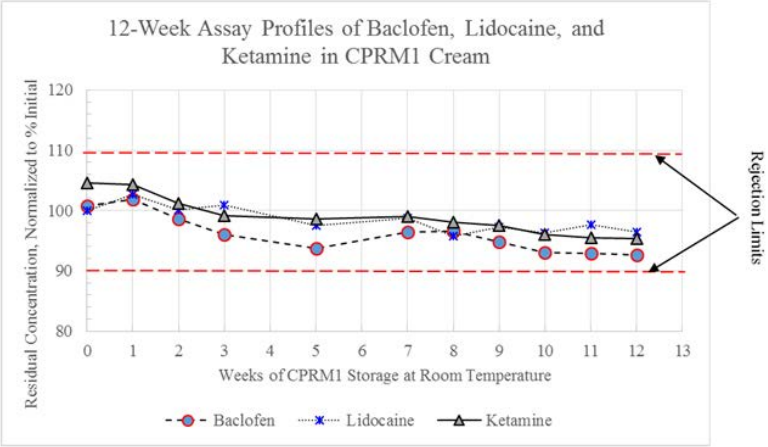

Figure 8: Twelve-week Assay profile of baclofen, lidocaine, and ketamine in CPRM1 cream, prepared in Lipoderm cream base

Acknowledgment

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Insight of a Counseling Pharmacist

By Margaret Tsopanarias, PharmD

My days as a retail pharmacist were not what I envisioned for myself as a pharmacist. They were rewarding in their own right, but I often felt like I spent more time doing routine, robotic work instead of changing and impacting patients' lives.

Through the misfortune of being laid off from my retail job to the fortune of finding my dream job of being an MTM pharmacist, I learned to appreciate the hefty importance of being a retail pharmacist.

Retail pharmacists are essentially gatekeepers of protecting and preventing medication problems before they begin (drug interactions, detecting incorrect dosages, medication misuse etc.). However, between dispensing medication, handling inventory, tending to phone calls with doctors, patients and insurance companies and now immunizing, pharmacists don't get a heck of a lot of time to sufficently counsel their patients. For most of us, that's the reason we became pharmacists in the first place.

When I became an MTM pharmacist, I now had the time to address problems that their pharmacy and/or doctor(s) have missed. Most plans allow this review to be completed annually. Being an MTM pharmacist means you get the opportunity to spend roughly half an hour reviewing a comprehensive list of patients' prescriptions and over the counter medications. You also have the opportunity to adequately review their drug allergies and medical conditions. You are essentially screening for drug interactions, therapeutic duplications, medication overuse/misuse, gaps in therapy and inappropriate or unnecessary medications. Issues do occur and they are often related to patients seeing multiple doctors, or patients being confused or overwhelmed and quite frankly, the pharmacy not having enough time to build a relationship with the hundreds or even thousands of patients they come across. I'm not shaming retail pharmacists or doctors. As a retail pharmacist, I may have let my fair share of potential problems slip through the cracks as well. This is why medication therapy management is so important and why it should be mandatory as a safeguard.

The following are some of the common issues I come across as an MTM pharmacist.

1. Inappropriate medications in elderly patients. Elderly patients are more susceptible to adverse drug reactions due to poor drug metabolism, comorbid disease states and concomitant medications. Medications that were once safe, start to become problematic.

2. 2.Inappropriate Beta Blocker selection for Heart Failure patients and/or patients not being aware they have heart failure

3. Therapeutic duplication with Ace inhibitors & Angiotension receptor blockers

4. Overuse of SABA (Short acting beta agonists)in Asthma or COPD

5. Misuse of long acting and short acting respiratory inhalers

6. Lack of Potassium monitoring when on mulitple medications that increase potassium
7. Chronic use of hypnotics such as Zolpidem without mention of proper sleep hygeine

8. Diabetic patients not being aware of signs and symptoms of high or low blood sugar and how to treat it

9. Inappropriate statin intensity selection based on cardiovascular risk factors

10. Poor medication compliance

Those issues mentioned above of course can be expanded upon and are just scratching the surface. For those of you that are retail pharmacists, I highly suggest you get your company to take MTM more seriously. You will feel rewarded and validated for improving the quality of lives of your patients. For those of you that are not pharmacists, I hope this article provides insight into the pharmacy world and empowers you to be more proactive with medication safety. If not for yourself, you may have an elderly family member or friend that can benefit from a comprehensive annual review of their medications. If your insurance company does not pay for this service, ask your pharmacist to carve out some time to provide extra counseling. In my experience, patients or caregivers forgo their complimentary medication review because their medications have not changed in several years. Please understand that guidelines and warnings on medications DO change. Even in cases where medication lists remain the same, an annual medication review is still important.

Cardiovascular Disease Risk Factors in South Asians: A Literature Review

The South Asian subcontinent consists of India, Pakistan, Bangladesh, Sri Lanka, and Nepal. In the United States, the South Asian demographic is the second largest Asian American group (1). Patients from this ethnic background make up a large percentage of all heart disease patients and have a higher rate of cardiovascular disease (CVD) compared to any other ethnic group (2). Studies have shown that South Asians develop heart disease 10 years earlier than other populations worldwide (3). Research of CVD in the South Asian population is sparse and very few studies have been conducted investigating its epidemiology or possible preventative measures in this community. The purpose of this review is to collect and review current pertinent data related to cardiovascular risk in the South Asian ethnic population.

CVD in the general population has been well-studied; common modifiable risk factors include hypertension, diabetes, hyperlipidemia, physical inactivity, diet, tobacco use, and obesity. In South Asians, these risk factors are prevalent; however in addition, findings show that their risk may be magnified. The limited research present sheds some data on the status of CVD in the South Asian population. A large, international case-control study by Joshi et. al found that the mean age for first myocardial infarction (MI) was significantly lower in South Asian subjects (53.0) than in subjects from other countries (58.8) (4). Another study by Swerdlow et. al investigates mortality in South Asian patients with insulin-treated diabetes compared to mortality in non South Asian patients in the general UK population. The study found that the standardized mortality ratio for South Asians diagnosed with diabetes before the age of 30 was 3.9 in men and 10.1 in women. Comparatively, the mortality ratio in non South Asian men and women was 2.7 and 4.0, respectively (5).

The Mediators of Atherosclerosis in South Asians Living in America (MASALA) study determined the ten-year atherosclerotic cardiovascular disease (ASCVD) predicted risk scores of 893 healthy South Asians living in the US. The study found that 49% of South Asian men and 13% of South Asian women had a high 10-year predicted risk. Additionally, almost three- quarters of South Asians were found to have a high lifetime predicted ASCVD risk (6). In a cross-sectional analysis of the MASALA study and another community-based cohort study, the Multi-Ethnic Study of Atherosclerosis (MESA), Kanaya et al compared South Asians to four other ethnic groups in the US (7). It was found that South Asians had a significantly higher age- adjusted prevalence of diabetes than the MESA ethnic groups (23%, compared to 6% in Caucasians, 18% in African Americans, 17% in Latinos, and 13% in Chinese Americans) (7).

Insulin resistance and β-cell dysfunction, hallmarks of diabetes, were also compared between the South Asian group and the other ethnic groups. Homeostasis model assessment (HOMA) was used to estimate insulin resistance and β-cell function. After adjustment for age and adiposity, HOMA of insulin resistance (HOMA-IR) levels were significantly higher and HOMA-β levels were lower in South Asians than in the other four ethnic groups (7). These results showed that South Asians may have impaired β-cell function and higher insulin resistance, which reduces the capability to compensate for higher glucose levels. This genetic mechanism is one that may account for the risk factor of diabetes in CVD.

Hyperlipidemia is another well-known risk factor for CVD. Abnormalities in lipoproteins in South Asians may contribute to their CVD risk. The INTER-HEART study, which explores global risk factors for acute myocardial infarction (AMI), found that the risk of AMI in South Asians is elevated at a much lower LDL-C level

compared with that of other ethnic groups (8,9). One proposed explanation for this mechanism is that smaller LDL particles are denser and may be more atherogenic, and South Asians carry a higher concentration of these smaller LDL particles at given LDL-C levels (9). In a study examining this risk factor, the presence of small dense LDL particles was found to be significantly higher in Asian Indians when compared with its presence in white subjects (10). LDL-C levels are a commonly used marker to determine CVD risk, and as such, recommendations for treatment may need to be revised for the South Asian population.

The INTER-HEART study also found that South Asians have lower levels of HDL-C, and, in addition, the protective effect of higher HDL-C levels seemed to be weaker for this group compared with other ethnic groups (9). High concentrations of smaller HDL particles may be to blame; small HDL particles are not as efficient in reverse cholesterol transport, which is important in cholesterol clearance. Studies have found that South Asians may have higher concentrations of small HDL particles, and lower concentrations of large HDL particles (9,11).

Another lipid abnormality associated with dyslipidemia in South Asians is elevated lipoprotein(a) [Lp(a)]. Apolipoprotein A, which is the active protein of Lp(a), is thought to adversely affect fibrinolysis due to its similarity to plasminogen (12). A few different studies by Anand et al found that Lp(a) levels in South Asians were higher than those in Caucasians (13). This genetic tendency for higher Lp(a) levels correlates with CVD risk. Patients with coronary heart disease (CHD) are shown to have about 5 times higher levels of Lp(a) than those of healthy patients (14). LDL-C levels are a commonly used marker to determine CVD risk, and as such, recommendations for treatment may need to be revised for the South Asian population. These findings on the lipid profiles of South Asians show that more research needs to be done in order to better understand dyslipidemia management in these patients, and further reduce CVD risk.

Other common risk factors for CVD are lifestyle habits, including diet and exercise routines. It is commonly believed that migration is a major risk factor for CVD. In a cross- sectional analysis using data from the MASALA study as well, acculturation was measured to determine whether or not it had a link to subclinical atherosclerosis (17). Traditional cultural beliefs were used as a tool to measure acculturation, with tertiles of strength (strongest, moderate, and weakest) as well. The results concluded that longer duration of residence in the U.S. was linked with higher levels of coronary artery calcium (CAC), which is a known predictor for CVD. Carotid intima media thickness (cIMT), which is used as a predictor for the extent of atherosclerotic disease, was also measured. It was found that lower (more beneficial) levels of cIMT were associated with those patients who had moderate traditional cultural belief only, and not those who had the strongest and/or weakest (15). The study hypothesizes that these lower levels are due to a healthier lifestyle adopted by these subjects, in which the more beneficial lifestyle behaviors from each culture (host and native) are taken up. However, more research needs to be done in this area to make further conclusions and determine interventions to reduce CVD risk.

Other important risk factors for CVD in South Asians are dietary patterns and nutrition choices. Using data from the MASALA study, Gadgil et al determined prevalent dietary trends in South Asians within the U.S. and related them to select risk factors for metabolic syndrome, like HDL, LDL, and HOMA-IR (16). Three major dietary patterns were identified: (1) animal protein, (2) fried snacks, sweets, and high-fat dairy, and (3) fruits, nuts, vegetables, and legumes. The animal protein dietary pattern was associated with higher total cholesterol and LDL levels. The second group (fried snacks, sweets, and high-fat dairy) was associated with higher HOMA- IR levels and lower HDL, whilst the third (fruits, nuts, vegetables, and legumes) was associated with lower odds of hypertension and lower HOMA-IR levels. Both the first two dietary patterns

showed adverse metabolic outcomes, and modifying these dietary choices may be a major key in reducing the risk of CVD in South Asian subjects.

In all patients with CVD, medication adherence and compliance is thought to be a major factor delaying disease progression. Research has shown that nearly 1 in 4 patients do not fill their medications after discharge from the hospital post-acute myocardial infarction (17). Additionally, of the patients who are initially compliant, up to 50% will discontinue their antihypertensive medications within 6 - 12 months (17). Medication adherence is also a factor that is thought to affect the CVD epidemic in the South Asian population.

In a systematic review of current evidence investigating adherence to cardiovascular medications in the South Asian population, data collected gives some insight into this subject. Only 17 studies were included in the final review, and adherence rates ranged from 32%-95% across studies (18). The reason for this large range could be because some studies used validated questionnaires like the Morisky Medication Adherence Scale (MMAS), while others used non- validated self-reported measures. Self-reported measures have a risk of recall bias, and therefore predictably had higher adherence rates. Studies that used validated measures had lower adherence rates, which suggest that there is a need for interventions to improve medication adherence rates in these patients.

In another systematic meta-synthesis review, adherence-related beliefs in patients of South Asian ethnicity were examined. The review included twenty-one publications related to medication adherence in the South Asian population, in disease states including CVD and diabetes. It was found that concerns about medication toxicity and beliefs in traditional remedies were both barriers to medication adherence (19). Adherence is compromised as these beliefs affect patient's perceptions of medication efficacy and necessity; these results are more noted among female South Asian patients than male. Patients were even shown to have delayed adherence to their medications in the hopes that the traditional remedies would be sufficient (19). The lack of knowledge among these patients needs to be addressed in order to help reduce CVD risk, and more research needs to be done in order to assess patient's medication adherence patterns.

Given the unique set of risk factors for CVD in the South Asian ethnic population, more resources need to be utilized in order to better understand these factors and their role in disease progression. As the current evidence suggests, in addition to having genetic predispositions that may lead to CVD, South Asians are also affected by traditional risk factors, such as medication adherence. Lifestyle behaviors, dietary intake, and cultural beliefs in this population also pose a unique challenge for healthcare professionals, and more research needs to be done in this area to better understand these challenges and how they can affect CVD risk.

The South Asian Heart Lifestyle Intervention (SAHELI) study is a recent pilot designed to evaluate healthy lifestyle interventions and their effects, if any, on reducing ASCVD risk in South Asian patients in the U.S. (20). The control group received translated printed education tools about ASCVD and healthy behaviors, while the intervention group attended six educational group classes, and received follow-up telephone calls. The results concluded that compared to the control group, the intervention group had significant weight loss, and greater sex-adjusted decrease in hemoglobin A1C after 6 months (20). The intervention group also participated in festive gatherings, which incorporated healthy activities like yoga, cooking lessons, and dance.
The SAHELI study shows some promise that culturally focused lifestyle interventions in the South Asian community may help reduce CVD risk. Further research in this area would be of benefit in order to help tackle CVD risk in this population.

More knowledge and research is needed about CVD in South Asians in order to better understand the unique risk factors that are present in this population. This focus would help healthcare professionals and communities take action in order to better control disease CVD progression in this population. The research on this subject so far shows that there is still more to investigate.

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Development and evaluation of Water dispersible tablets of Acyclovir

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Development and Evaluation of Water Dispersible Acyclovir Tablets

ABSTRACT

Objective: The present investigation was design to develop a water dispersible tablet of Acyclovir for enhancing its onset of action using some superdisintegrating agents as it shows poor water solubility.
Materials and Methods: The acyclovir water dispersible tablet was prepared by using Veegum F (Magnesium Aluminum Silicate) and Sodium Starch Glycolate as superdisintegrating agent, Avicel PH 102 as a diluent, Povidone K30 as a binder and carried out studies for weight variation, thickness, hardness, content uniformity, disintegrating time, dispersion time, wetting time and in vitro drug release. Tablets were prepared by using wet granulation method.
Results and Discussion: Five different formulations of acyclovir dispersible tablet were prepared. Out of five, formulation F2 exhibited drug release 85.11% and formulation F4 showed highest drug release 85.42% in 10 min. These two preparations also exhibited the shortest wetting time 57.56 and 54.46 second with dispersion time 78 and 110 second respectively.
Conclusion: It was concluded that acyclovir water dispersible tablets with enhanced dissolution rate can be formulated using selective superdisintegrants in a view to obtain more bioavailability, therapeutic effect and patient compliance.

Key words: Acyclovir, Water Dispersible Tablet, Superdisintegrants, Dispersion Time

INTRODUCTION

For most therapeutic agents used to produce systemic effects, the oral route still represents the preferred way of drug administration, owing to its several advantages and high patient compliance compared to many other routes. [1] Most of the oral pharmaceutical dosage forms like conventional tablets and capsules are formulated to be swallowed or chewed. As results children, bedridden patients and elderly patients have difficulty in swallowing these dosage forms. [2-3] To overcome this drawback novel drug delivery systems like orally disintegrating tablets have been developed[4] which disintegrate / dissolve/ disperse in saliva within few seconds without water. It becomes difficult to administer conventional tablet to patients. But administration of water dispersible tablets make the treatment becomes easier. Therefore, water dispersible tablets of this drug were considered. United States Food and Drug Administration (USFDA) defines water dispersible tablets as "A solid dosage form containing medicinal substances or active ingredient which disintegrates rapidly usually within a matter of seconds when placed in water".[5] The major advantage of the water dispersible tablets formulation is that it combines the advantages of conventional tablet formulations, thus allowing the ease of swallowing provided by the liquid formulation.

Acyclovir is a guanosine analogue, one of the most commonly used antiviral drugs, it is primarily used for the treatment of *Herpes simplex* virus infections, as well as in the treatment of *Varicella zoster* (chickenpox) and *Herpes zoster* (shingles). It was originally extracted from a Caribbean sponge. It is selectively converted into Acyclovir-guanosine mono-phosphate (Acyclovir-GMP) by viral thymidine kinase, which is far more effective (3000 times) in phosphorylation than cellular thymidine kinase. Acyclovir is poorly water soluble and has poor oral bioavailability (15–30%), hence intravenous administration is necessary depending on the clinical condition of the patients, if high concentrations are required. When orally administered, peak plasma concentration occurs after 1–2 hours. Acyclovir has a high distribution rate; protein binding is reported to range from 9 to 33%.[6] The elimination half-life of Acyclovir is approximately 3 hours. It is renally excreted, partly by glomerular filtration and partly by tubular secretion. The present study was designed to formulate water dispersible tablets of Acyclovir and pharmaceutically acceptable acid addition salts thereof in a view to solve some of the problems encountered in administration of drug to pediatric and elderly patients.

MATERIALS AND METHODS

Materials

Acyclovir BP (China national native produce Ltd), Veegum F (Colorcon Asia Pvt. Ltd, USA), Sodium Starch Glycolate (Taiwan, Chunghwa chemical synthesis & Biotech co Ltd), Povidone K30 (Colorcon Asia Pvt. Ltd, USA), Avicel PH 102 -Microcrystalline cellulose (Mingtai Chemical Ltd. Taiwan), Magnesium Stearate (Remo Chemical Ltd. Bangladesh) and Talc (Remo chemicals, Bangladesh).

Equipments

Rapid Mix Granulator, # 25 Mesh Screen, Rotary Tablet Punch (8 station), Tablet Hardness Tester (YD-1 hardness tester), Friability Tester (Electrolab EF-1), Electrolab Tablet Dissolution Test Machine (08L), Electronic Balance, Double Beam UV Spectrophotometer, Karl Fischer Instrument, Tap Density Tester.

Preparation of matrix tablet [7]

Tablets were prepared by wet granulation method. The drug (Acyclovir) and excipients such as Veegum F, So-

dium Starch Glycolate, Avicel PH 102 were mixed properly in poly bags and were granulated with Povidone K30 was dissolved in 50% aqueous alcohol (Ethyl Alcohol) as granulating agent. The resultant granules were dried in a tray drier at a temperature of 700C for approximately 25 minutes. The granules were then shifted through a 1000 µm diameter mesh sieve dry granules were lubricated with magnesium stearate and talc. The matrix tablets were prepared by compression using 8 station rotary machine (Kambert Machinery). Each tablet contained 800 mg drug (Table 1).

Table-1: Formulation of Acyclovir Tablets (F-1 to F-5)

		Formulations				
Ingredients	**Justification**	**F1**	**F2**	**F3**	**F4**	**F5**
Acyclovir BP	Active Ingredient	800	800	800	800	800
Avicel Ph 102	Tablet diluents	76	74	76	76	66
Veegum F (Magnesium Aluminum Silicate)	Dispersing Clay	53	60	55	50	55
Sodium Starch Glycolate	Disintegrant	40	35	35	40	45
Povidone K30	Superdisintegrant	15	15	20	20	18
Magnesium Stearate	Tablet lubricant	10	10	8	8	10
Talc	Tablet lubricant	4	4	4	4	4
Citric acid	Flavor enhancer & helps breakdown of tablet in water	2	2	2	2	2
Total weight (in mg)	**1000**	**1000**	**1000**	**1000**	**1000**	**1000**

Evaluation of physical properties of formulation granules [8, 9]

Bulk density

Apparent bulk density (ρb) was determined by placing presieved drug excipients blend into a graduated cylinder and measuring the volume (Vb) and weight (M) "as it is".

$$\rho b = M/Vb$$

Tapped density

The measuring cylinder containing a known mass of blend was tapped for a fixed number of taps. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (ρt) was calculated using following formula.

$$\rho t = M/ Vt$$

Compressibility index

The compressibility index of the granules was determined by Carr's compressibility index:

$$\text{Carr's index (\%)} = [(TBD - LBD) \times 100]/TBD$$

Total porosity

Total porosity was determined by measuring the volume occupied by a selected weight of powder (Vbulk) and the true volume of granules (the space occupied by the powder exclusive of spaces greater than the intermolecular space (V).

$$\text{Porosity (\%)} = (Vbulk - V) / Vbulk \times 100$$

Angle of repose

The angle of repose of granules was determined by the funnel method. Accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

Angle of repose, $\theta = \tan^{-1}(h/r)$

Where, h = Height in cm of the powder cone, r = Radius in cm of the powder cone.

Moisture content

Moisture content of granules was determined using Mettler Karl Fischer Titrator. About 120mg granules was weighed and added into the reagent solutions of the instrument, which was stirred and the tare weight was fed into the instrument. Then after certain duration of time the moisture content as % w/w was read on the monitor.

Hausner Ratio

Flow property, a very important parameter to be measured since it affects the mass of uniformity of the dose. It is usually predicted from Hausner ratio and angle of repose measurement. Hausner ratio is determined from the following equation-

Hausner Ratio = Tapped Density/Bulk Density

Evaluation of physical properties of Acyclovir matrix tablets

Weight variation test

To study weight variation, 20 tablets from each formulation were weighed using an electronic balance and the test was performed according to the British Pharmacopoeia.

Hardness

For each formulation, the hardness of 6 tablets was determined using Monsanto hardness tester.

Friability

Friability of 6 tablets of each proposed formulations were determined using the Friability tester.

Surface area

As the shape of the tablet was round flat, so it can be compared with a cylinder. Surface area of a cylinder is calculated by using the following equation:

Cylinder surface area = $\pi r2h$

Where, r = Radius in mm of tablet and h= thickness in mm of the tablet.

Drug content [10]

Two tablets were powdered and the blend equivalent to 800 mg of Acyclovir was weighed and dissolved in suitable quantity of 0.1 N hydrochloric acid of pH (1.3). The solution was filtered, suitably diluted and the drug content was analyzed spectroscopically at 255 nm. Each sample was analyzed in triplicate.

Water absorption ratio

A piece of tissue paper was folded twice and placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting was recorded. The wetted tablet was then weighed. Water absorption ratio R, was determined using the following equation:

$$R = 100\ (Wa - Wb)/Wb$$

where Wb is the weight of tablet before water absorption and Wa is the weight of tablet after water absorption.

Wetting time [11]

A piece of tissue paper (10.75×12 mm) folded twice was placed in a culture dish (d=6.5 cm) containing 6 ml of water. A tablet was put on the paper and the time for complete wetting was recorded.

***In vitro* dispersion time [12]**

Tablet was added to 10 ml of phosphate buffer solution (pH 7.4) at 37±0.5°C. Time required for complete dispersion of a tablet was recorded.

***In vitro* release studies of Acyclovir tablets**

Dissolution studies were conducted to determine the release pattern of the drug from the product. Dissolution test for Acyclovir was carried out as per USP method for dissolution test for tablets and capsules using apparatus II (paddle type). Dissolution medium used was 900 ml of 0.1 N hydrochloric acid (simulated gastric fluid, pH 1.3) rotating at 50 rpm at 37±0.50C. An aliquot of 10 ml of samples were withdrawn at different time periods and replaced with fresh medium. These samples were filtered and diluted. Absorbance of the resulting solution was measured at 255.0 nm (experimental λ_{max} for Acyclovir in pH 0.1 N hydrochloric acid). Percent drug release was calculated.

RESULTS AND DISCUSSIONS

Acyclovir dispersible tablets were prepared by wet granulation method. The excipients such as Veegum F, Sodium Starch Glycolate, Avicel PH 102, Povidone K30, magnesium stearate, talc and citric acid were mixed properly in different stages of the formulations containing acyclovir 800 mg (table 1). The physical properties of the granules were studied in terms of loose bulk density (0.327 – 0.394), tapped bulk density (0.315 – 0.412), angle of repose (25.61 – 27.95) and moisture content (0.926 – 1.014). The particle size of the blend granules was on an average of 700 μm and flow property was determined by Hausner ratio (1.18-1.22) and Carr's index (15.48-17.72) (table 2).

Table-2: Physical properties of Acyclovir granules (F-1 to F-5)

Formulation	Loose Bulk Density (LBD) (gm/ml)	Tapped Bulk Density (TBD) (gm/ml)	Carr's Index (%)	Hausner ratio	Angle of repose (0)	Moisture content (%)
F-1	0.327	0.359	16.51	1.20	27.95	1.014
F-2	0.298	0.315	15.68	1.19	25.61	0.963
F-3	0.336	0.394	15.48	1.18	29.19	1.003

F-4	0.339	0.402	16.07	1.19	25.67	0.930
F-5	0.394	0.412	17.72	1.22	27.47	0.926

The dispersible tablets were prepared by compression using 8 station rotary machine (Kambert Machinery). The tablets of different formulations were subjected to various evaluation tests, such as weight variation, friability, hardness, thickness and content uniformity according to procedure specified in British Pharmacopoeia 2010. The weight variation of the tablets from all batches varied between 0.38-0.58%, thickness between 8.89-8.97 mm and hardness 4.12- 5.2 N as shown in table 3. Friability of tablets from different batches showed below 1.87%. Drug content was found to be high (≥98.86%) in all the tablet formulations. Thus wetting times and dispersion time of tablets was found to be of all tablets from different batches shown to be satisfactory (table 3 and fig-1).

Table-3: Physical properties of Acyclovir tablets (F-1 to F-5)

Formulations	Average weight (mg)	Diameter (mm)	Thickness (mm)	Hardness (N)	Friability (%)	Dispersion time(S)	wetting Time(S)	Drug Content (%)	Water absorption ratio
F-1	1022±0.17	10	8.97±0.01	4.12±0.04	1.87	158	57.43	99.31	1.3
F-2	1018.1±0.11	10	8.93±0.02	4.3 ± 0.07	0.76	78	57.56	99.43	1.7
F-3	1017.8±0.15	10	8.90±0.02	4.5 ± 0.05	1.36	144	56.23	99.12	1.2
F-4	1019.5±0.08	10	8.92±0.01	.32±0.02	1.1	110	54.46	99.56	1.5
F-5	1020.05±0.09	10	.89±0.01	5.2 ± 0.04	1.42	110	55.56	98.86	0.98

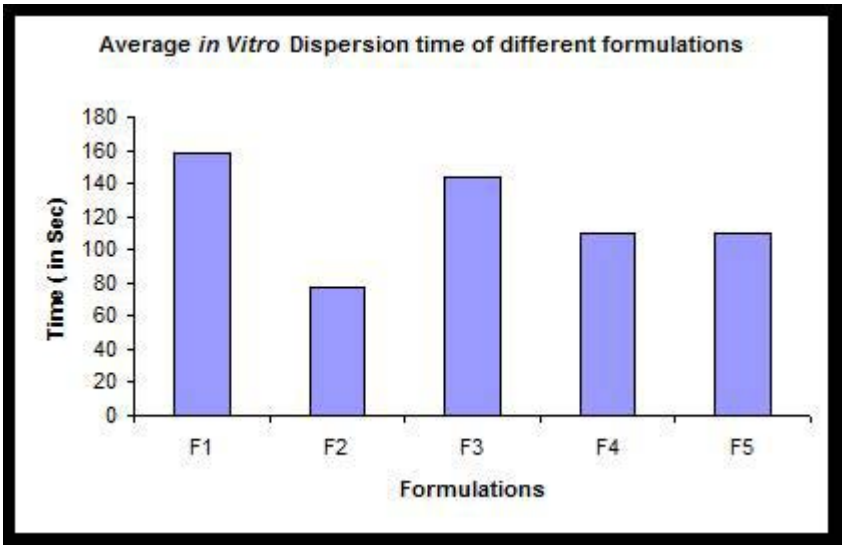

Fig 1: Comparative *In Vitro* Dispersion time of Acyclovir water dispersible tablets

All tablets found satisfactory release profile (table 4). The influence of superdisintegrants on the dissolution of Acyclovir from the tablets was shown in fig - 2. The drug release in 10 min and 25 min was increased with

increasing level of Veegum F and Povidone K30. However values decreased with increase in the level of sodium starch Glycolate. Out of five formulations F2 and F4 formulation exhibited the best drug release 85.11% and 85.42% in 10 min and cumulatively 88.38% and 89.01% in 25 min respectively (Table 4). In the study, the relatively larger fragments generated by tablets were not small enough to pass through

Table 4: Percentage (%) of release of five formulations (F-1 to F-5) of Acyclovir tablets

	Cumulative percentage (%) of drug release				
Time (in Min)	F1	F2	F3	F4	F5
0	0	0	0	0	0
10	81.63	85.1	79.42	85.42	81.32
15	85.24	87.14	80.82	87.46	82.71
20	85.70	87.92	81.27	88.55	83.80
25	86.47	88.38	82.35	89.01	84.25

the screen of the dispersion vessels. The percent drug release of all the batches was found to be between 79.42 to 89.01 % within 10 to 25 minutes. Comparative dissolution profile of all batches (F1to F5) is given in fig - 2. It was observed that as the concentration of superdisintegrants increased the drug release also increased.

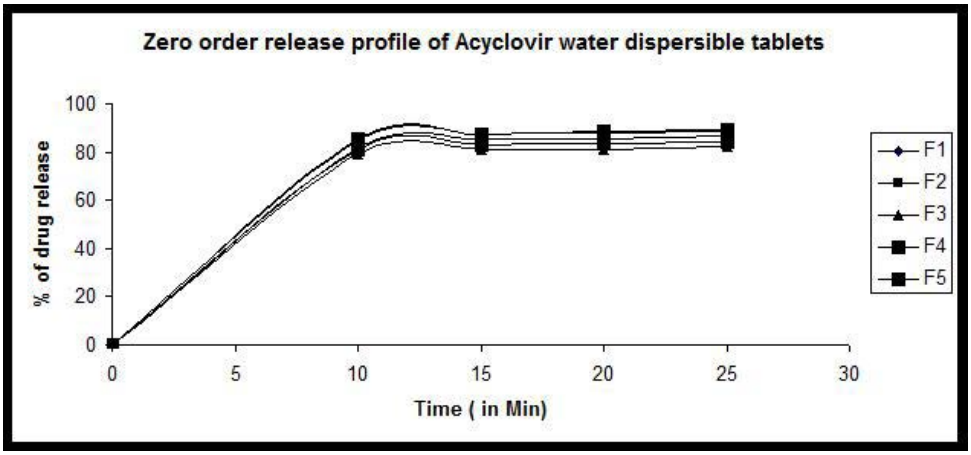

Fig 2: Zero order release kinetics of Acyclovir water dispersible tablets

The various technologies used to prepare water dispersible tablets include direct compression, wet granulation, sublimation, tablet moulding, spray drying, and freeze drying and mass extrusion. The fast disintegration and dissolution effect of water dispersible tablets mainly depends on the type of superdisintegrants used in the tablet formulation. [13] According to product information provided by the manufacturers of superdisintegrants, the excipients should be used in amount of 1-8% or with amount of about 2% to 4% being indicated as optimal. [14] Most commonly used superdisintegrants include sodium starch Glycolate, croscarmellose sodium (cross linked carboxymethylcellulose), cross povidone (cross linked Povidone) [15]. Use of Veegum F and sodium starch glycolate in combination mainly reduces the disintegration and dissolution time of acyclovir water dispersible tablets. From the comparative dissolution profile of all batches (F1to F5) of the dispersible tablets it was observed that as the concentration of superdisintegrant is increased the drug release form

the tablet is also increased. Among the batches F2 and F4 were the best considering the highest percentage of drug was released within 10 min and exhibited the shortest wetting time 57.56 and 54.46 second with dispersion time 78 and 110 second respectively.

CONCLUSIONS

The results obtained suggest that water dispersible tablets of Acyclovir containing Veegum F and Sodium Starch Glycolate can successfully be formulated with low concentration. Among the formulations, batch F2 and F4 showed superior micromeritic properties along with excellent in vitro dispersion time and drug release as compare to other formulations. It was concluded that addition technique of superdisintegrants is a useful technique for preparing dispersible tablets by wet granulation method. Rapid absorption, improved bioavailability, effective therapy and better patient compliance may be predicted from such acyclovir water dispersible tablet formulation.

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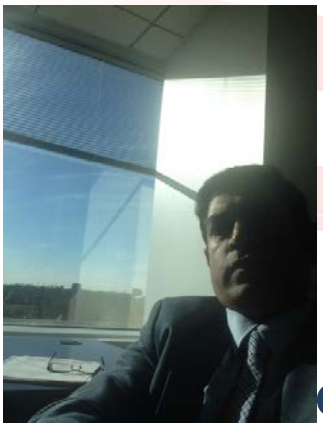

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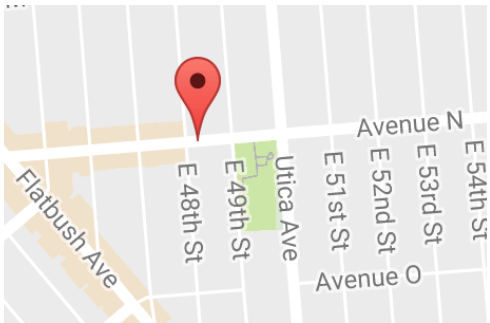

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