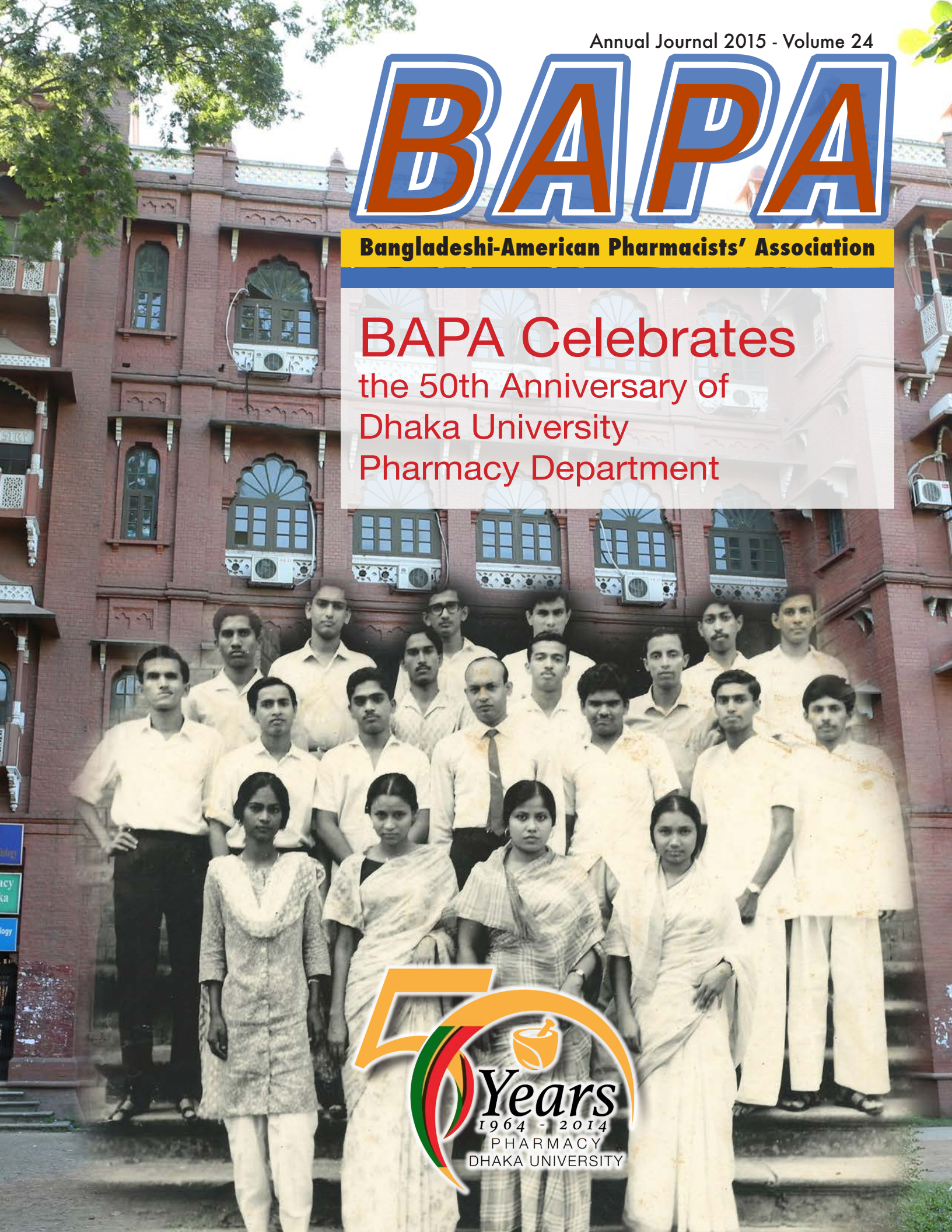
Annual Journal 2015 - Volume 24

BAPA

Bangladeshi-American Pharmacists' Association

BAPA Celebrates
the 50th Anniversary of Dhaka University Pharmacy Department



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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
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Md. Lutful Haque
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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

24th Annual Convention Programs

August 28th, 29th and 30th, 2015

STOCKTON SEAVIEW HOTEL AND GOLF CLUB

401 S New York Rd. Galloway, NJ 08205

BAPA CONVENTION SCHEDULE AT-A-GLANCE

Day 1	Friday, August 28, 2015
2:00 PM - 8:00 PM Hotel Lobby	Registration
6:00 PM - 8:00 PM Salon B	**Bridging the Gap- The Role of Pharmacists in Underserved Care** Dr. Jennifer S Bhuiyan, PharmD Pharmacist at Johnstown Free Medical Clinic, Johnstown, PA
8:00 PM - 10:00 PM Bayview Ballroom	Dinner
10:00 PM - 1:00 AM	Cultural Program by Various Artists

Day 2	Saturday, August 29, 2015
8:00 AM - 10:00 AM Main Dining Room	Breakfast
8:30 AM - 10:00 PM Salon B	**Still Struggling to Breathe: COPD Pharmacotherapy Update** Dr. Charnicia E. Huggins, PharmD. Assistant Professor of Pharmacy Practice at Touro College of Pharmacy in Harlem, NY
10:00 AM - 10:45 AM Harding Room	**VENDOR SHOWCASE** with Coffee Break
10:45 AM - 11:15 AM Salon B	**US Biosimilar Products- A Regulatory Overview** Naushad Shoaib Islam, MS Global Regulatory Leader, Oncology TA Johnson & Johnson. Adjunct Associate Professor, School Of Pharmacy Long Island University, NY
	Prayer Room: Cape May and Reeds | Saree Vendor: Eisenhower Room

11:15 PM - 1:15 PM Salon B	**The Spectrum of Understanding Obesity: Considerations and Options** Dr. Shushama Alam, Pharm.D. Medical Science Liaison at Vivus, Inc, Mountain View CA
1:15 PM - 2:30 PM Bayview Ballroom	**Lunch**
2:30 PM - 3:00 PM Salon B	**An Integrative Approach to CardioMetabolic Dysfunction** Dr. Ilora Rafique M.D.
3:00 PM - 3:30 PM Salon B	**Advanced Care Planning** Maleka Z. Ahmed M.D.
3:30 PM - 5:30 PM Salon B	**Managed Care 101: A Pharmacist's Perspective** Dr. Tasmiya Khan, PharmD Consultant at BluePeak Advisors
7:30 PM - 9:30 PM Bayview Ballroom	**Dinner and Reception** Program (Formal Attire) - Opening of program by General Secretary - Vice President thank you note - Welcome note by the President - Brief comment by our Platinum Sponsors (Kinray and RDC) - Recognition of new graduates and pharmacists - Keynote speech by Roger Paganelli, PSSNY President
9:30 PM - 2:00 AM Bayview Ballroom	**Cultural Program**

Day 3	**Sunday, August 30, 2015**
8:00 AM - 10:00 AM Main Dining Room	**Breakfast**
10:00 AM - 11:30 AM Salon B	**Finding Quick and Lasting Relief from Breathlessness: Asthma Pharmacotherapy Review** Dr. Charnicia E. Huggins, PharmD. Assistant Professor of Pharmacy Practice at Touro College of Pharmacy in Harlem, NY
12:00 PM	**Check Out**

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

Prayer Room: Cape May and Reeds | Saree Vendor: Eisenhower Room

Message from the PRESIDENT

Mohammad
IQBAL RASHED

We are very proud to state that we have celebrated Golden Jubilee of Pharmacy education in Bangladesh. Congratulations all of you and welcome to the 24th Annual BAPA Convention of 2015.At this occasion, let's spell out the journey of Pharmacy education in USA and Bangladesh.

In USA, the history of pharmacy education is very interesting, the first college to train pharmacists was founded in 1821 as the Philadelphia College of Pharmacy. Impetus for this came from a plan by local physicians to start training pharmacists. Local pharmacy leaders were outraged that physicians would presume to be able to train pharmacists. Hence, the pharmacists were motivated to start their own program. Boston Pharmacists shortly followed in 1823 with the second College, the Massachusetts College of Pharmacy, now, The Massachusetts College of Pharmacy and Health Sciences. Over the years, four years baccalaureate degrees were instituted as norm, eventually, by the late 1990'S, the profession had moved to a six year Doctor of Pharmacy (Pharm-D) degree as a standard.

On the contrary, Pharmacy education in Bangladesh started since 1st July, 1964 at the University of Dhaka under the supervision of Professor Emeritius Dr. Abdul Jabber. At present, there are six public universities and 22 private universities who are offering professional pharmacy degree. However, practice of pharmacy and health care delivery system, professional ethics, social and behavioral pharmacy are ignored in Bangladesh. Since, Pharmacists play very important role in drug distribution and dispensing, patient safety, clinical program development, communication with patients, prescribers, and pharmacists, and drug benefit design. Therefore, to establish Hospital Pharmacy and community pharmacy, the role of Pharmacists in Bangladesh has to be evaluated, reshaped and remodeled. By bridging the gap, Doctor of Pharmacy/Pharm-D program has to be started as well. This is the demand of today. This will bring new edge and dimension in the professional.

On a serious note, I would like to congratulate and welcome all new generation Pharmacists to BAPA. We count on your leadership to bring changes and new dimensions to our esteemed organization.

Finally, I would like to thank all our sponsors, patrons, fellow members and executive committee for continued support.

Thank you.

Mohammad Rashed, R.Ph., Pharm.D.
President, BAPA

Message from the VICE PRESIDENT

Mohammed
SHABBIR TAHER

Dear BAPA members,

Welcome to our annual convention. As always I feel honored to serve this great organization and its members.

Last two years have been simply remarkable. Under the supervision of our president Mohammad Rashed we held dinner cruise for the first time, organized prayers for the entire community and our new generations of pharmacists are now more engaged and committed to serve this organization for many years to come.

The next few years we will see more from the new generation taking on active leadership roles, therefore we need your continuous support and guidance as we head towards a new era.

Hope everyone enjoys the rest of the convention.

Thank you.

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

Message from the GENERAL SECRETARY

Mohammed
MOHIUDDIN

Every year, it's that time of the year again for which we all are very much looking for, which we name, BAPA Annual Convention. I am excited to welcome to all participants, peers, new generation pharmacists, distinguished guests, friends and families at the 24th Annual BAPA Convention, 2015.It is indeed a remarkable time for all of us because we will have the opportunities for networking, exchange of views and ideas among peers, colleagues, and fellow members.

BAPA being a revered professional organization, the fascinating, enlightening professional continuing education and pharmaceutical scientific seminars have been arranged and should be conducted by renowned professionals and academicians for professional enrichment. There are exciting cultural programs for our family members.

It is obvious that it requires a lot of sincere effort and resources to organize a convention. This is our 24th convention. This became possible due to active participation of an unlimited number of our fellow members that makes BAPA a vibrant and positive organization.

Furthermore, I am excited to congratulate and welcome all new generation Pharmacists to BAPA. We shall appreciate their sincere effort and leadership to bring changes for professional development and new dimension to our esteemed organization.

Finally, I would like to thank all participants, peers, our sponsors, patrons, advertisers and executive committee members for their continued support. I wish you all a most enjoyable and successful convention, 2015.

Best wishes

On behalf of the executive committee

Md Mohiuddin, B-Pharm(Hons), M-Pharm.
General Secretary, BAPA

Message from the TREASURER

Fahim
AHMAD

Thank you for giving me the opportunity to serve as BAPA Treasurer. It is an exciting time for BAPA as we look to bring new ideas in while maintaining what has made this organization great for so many years. Much credit must be given to the President and Vice President for organizing this convention.

I hope to maintain the level of excellence of those that came before me while creating a new path as we move towards the future.

This is an exciting time for BAPA as the convention is always a wonderful opportunity to meet new people, eat good food, and earn continuing education credits. Every year we have a nice mixture of pharmacists from different environments - from administration, clinical, hospital, retail, industry, and many more.

I look forward to finishing up work with the current committee and best of luck to those that follow.

Thank you

Fahim Ahmad, R.Ph., Pharm.D.
Treasurer, BAPA

Articles

Articles

BIOEQUIVALENCE STUDY OF TWO OMEPRAZOLE FORMULATIONS "PROCEPTIN® " AND "LOSEC® IN BANGLADESHI HEALTHY SUBJECTS

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Keywords: Omeprazole, cross-over design, HPLC, bioequivalence study, generic preparation

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Abstract

The bioequivalence study of two omeprazole formulations Proceptin® 20mg capsule and Losec® 20mg MUPS tablet were compared in healthy subjects. The study was an open-label, randomized, two-treatment, two-sequence, two-way crossover, single-dose study conducted under fasting conditions with a wash out period of fifteen days between the two administrations. Blood samples were collected pre-dosing and at 0.5–24.0 h post administration of a single oral dose of either of the formulation followed by HPLC analysis. Twenty-eight healthy male subjects (20-28 years) participated in the study. Only four subjects dropped from the study and other 24 completed the study and were included in the pharmacokinetic and statistical analysis. Evaluated mean (±SD) values of the pharmacokinetic parameters for reference and test products were C_{max}; 345.28 (±42.38) and 316.23 (±26.12) ng/mL, t_{max}; 2.28 (±0.16) and 2.69 (±0.23) h, AUC_{0-24}; 710.01 (±92.51) and 771.13 (±102.35)

h-ng/ml and $AUC_{0-\infty}$; 848.21 (±65.31) and 902.56 (±45.23) h.ng/mL, respectively with no significant (p>0.05) differences in paired t-test. Moreover, 90% CI for the AUC_{0-24}, and C_{max} values were 89.245–103.154% and 81.634–102.211% respectively is within the predetermined FDA bioequivalence range of 80–125%. On the basis of the pharmacokinetic parameters AUC_{0-24} the relative bioavailability of the test preparation Proceptin 20 capsule was 108.61% of that of the reference preparation Losec 20mg MUPS tablet. This study stipulated that, the test and reference formulations of omeprazole meet the regulatory criteria for bioequivalence. Thus the test product Proceptin® 20mg may be supplanted for reference product Losec® 20mg MUPS tablet in oral administration.

Introduction

Omeprazole, a substituted benzimidazole, is one of the most widely prescribed drugs internationally and over the counter drug in some countries. As a pro-drug after conversion to its active form in the parietal cell it binds irreversibly[1] with H^+/K^+-ATPase (the gastric proton pump), which causes an effective and long-lasting inhibition of gastric acid secretion.[2-4] Therefore, omeperazole is widely used in the treatment of active duodenal ulcer, gastro-esophageal reflux disease (GERD), erosive esophagitis, active benign gastric ulcer, Zollinger-Ellison syndrome, infection of *Helicobacter pylori* as part of combination regimens and or other pathological hypersecretory conditions. [5-6]

From a pharmacokinetic perspective, omeperazole is absorbed rapidly, and systemic availability in humans is approximately 60% after an oral dose of a 40 mg capsule, which indicates a fairly extensive first-pass metabolism. [7] The protein binding of omeperazole in human plasma is about 95%. [8-9] It is metabolized into 5-hydroxyomeprazole and omeprazole sulfone by CYP2C19 and CYP3A4, respectively and the overall metabolism of it depends more on the activity of CYP2C19 than that of CYP3A4. [10-12] The 5-hydroxyomeprazole is more than 100 times less potent than omeperazole, and the omeperazole -sulphone does not possess any antisecretory activity.[8] Omeperazole is eliminated by metabolism with a mean plasma $t_{1/2} \leq 1.0$ h. In healthy individuals, about 80% of a given dose is excreted as metabolites in the urine and about 20% in the feces. [7-9]

The multi unit pellet system (MUPS) tablet is a patented formulation of omeperazole designed to optimize delivery of omeperazole to the site of its absorption in the small intestine. In particular, the gastro-resistant properties of the multiple layered micropellets are important to protect the acid-labile omeperazole from gastric juices. Since omeperazole is not stable at acidic pH, enteric-coated formulations are administered and therefore, wide variability in the absorption of formulations of this drug may exist owing to differences in coating which may influence protection against the acid and, consequently, may affect bioavailability.[13,14] Enteric-coated formulations of omeperazole reached mean maximal concentration ranging from 400 to 800 ng/ml [15-19] demonstrating its wide pharmacokinetic variability.

Hence, the purpose of this study was to determine the various pharmacokinetic parameters such as maximum plasma concentration (C_{max}) at the time (t_{max}), area under the plasma concentration time curve (AUC_{0-t}), area under plasma concentration time curve up to infinity ($AUC_{0-\infty}$), plasma elimination rate constant (k_{el}), the plasma elimination half life ($t_{1/2}$) after oral administrations of omeprazole enteric coated pellet formulations Proceptin® 20mg capsule and Losec® 20mg MUPS tablet to evaluate the bioequivalence of two formulations.

Materials and methods

Drugs and reagents

Two commercially available brands of 20 mg omeperazole, Proceptin® capsule (test preparation); Batch No: SUL067, DAR No: 186-98-34 manufactured by Beximco Pharmaceutical Ltd. Dhaka, Bangladesh and Losec® 20mg MUPS tablet (reference formulation); Batch No: MK11085 manufactured by Astra Zeneca, Sweden containing omeperazole magnesium. Omeperazole (98.97% purity), used for the preparation of Proceptin® capsule were collected from the manufacturer for analysis and method development; and pantoprazole (96.98% of purity), used as an internal standard were purchased from Reddy's Laboratories Ltd. (Hyderabad, India). Deionized water was prepared using Milli-Q system (Continental Water Systems, El Paso, TX, USA). E. Merck (Darmstadt, Federal Republic of Germany) supplied HPLC grade methanol. Other reagents used were of analytical grade.

Subjects

Twenty-eight healthy male Bengladeshi subjects aged 20-28 y and body mass index ranging from 17.5 to 23.65 kg/m^2 participated in this study. None of the subjects was an alcohol user, drug abuser, concomitant medication user and smoker during the period of the study. Demographic data was collected from all the participants who gave written consent after reading the protocol approved by the Bangladesh Medical research Council (BMRC).

Study Design

An open label, randomized, two-way, crossover study was designed. There were two dosing sessions with a 15 d washout period. All the volunteers were required to participate in two dosing sessions with a wash out period of seven days between the two administrations. In each dosing session, volunteers received either the test preparations or reference preparations as a single dose, only on the study day, as per the randomization code at a fixed time. Volunteers were in fasting condition before drug administration. The study preparations were allowed to ingest with 200mL of water. Standard breakfast, lunch, snack and dinner were served at 2, 5, 8 and 12 hours of post-drug administration respectively in each period of the study. Volunteers were given code numbers. They were allocated to the treatment (reference or test preparation) in accordance with the randomization code. Neither the personnel in charge of the determination of plasma levels nor the physician and nursing staff in charge was informed of the sequence of administration.

Ethical review and consent procedure

Guidelines as drawn up by the Bangladesh Medical Research Council (BMRC) were followed with regard to the treatment of human volunteers in the study. These guidelines met the requirements of the U.I S. Code of Federal Regulations (Title 21, Part 56), the Declarations of Helsinki [20] and the Canadian MRC Guidelines. The protocol containing the aims and objectives, and research procedure was submitted for ethical clearance and was approved by BMRC (number: BMRC/NERC/DO 2010-2013/1019 date 05.08.2012). All the participants were informed about the nature and purpose of the study with expected outcome being a participant. For assurance of the complete understanding of the subjects, a written consent form was obtained from each participant included in the study.

Blood Sampling

An indwelling -intravenous catheter (Vasofix, Germany) was inserted into a suitable forearm vein with strict aseptic precautions for blood sampling. Five ml of blood were withdrawn during each time and were collected by a nurse prior to dosing at 0 min (baseline) and 0.5, 1.0, 2.0, 3.0, 5.0, 8.0, 12.0, and 24.0 h after dosing. Heparinized blood samples were centrifuged for 25 min after collection at 3500 rpm for 20 min at 2-8^{o}C. Plasma was separated and stored at -80° C until analysis.

Sample preparation

One ml of plasma sample was mixed with 100 µl of methanol: acetate buffer (pH 4.6, 1:4 v/v) mixer followed by further mixing with 5.0 ml of dichloromethane: acetonitrile (4:1 v/v). The blend was vortexed for 30 sec. Again, after centrifugation at 4500 rpm for 10 min, 4.0 ml of organic phase separated and evaporated under a nitrogen stream. The residue was dissolved in 200 µL of mobile phase and 100 µL of it was injected into the HPLC chromatographic system.

Chromatographic analysis

Shimadzu Prominence (Kyoto, Japan), an HPLC system that consists of a SCL-20 AVP system controller with two pumps (Kyoto, Japan), determined the omeperazole and internal standard pantoprazole plasma levels. Separation of compounds was carried out by Luna C_{18} column (5µ, 4.6 × 250 mm) (Phenomenex, Torrance, California, USA) eluted with water and acetonitrile (58:42, v/v) at room temperature at a flow rate of 1.0 ml/min. Ultraviolet detection was achieved with SPD-20AVP UV-VIS detector (Shimadzu Corporation; Kyoto, Japan) at 302 nm.

Pharmacokinetic analysis

Plasma drug concentrations at defined time points of the study were used in pharmacokinetic calculations. Pharmacokinetic parameters were derived for both test and reference product. Data set was prepared for the estimation of pharmacokinetic parameters by using program kinetica (version 4.4, Adept Scientific, UK) followed by non-compartmental method of analysis. The pharmacokinetic parameters included were maximum

plasma concentration (C_{max}), time to reach the maximum concentration (t_{max}), half-life ($t_{1/2}$), area under the plasma concentration-time curve up to last quantifiable time (AUC_{0-24}), area under the plasma time curve up to time infinity ($AUC_{0-\infty}$), elimination rate constant (k_{el}), mean residence time (MRT), area under the moment curve up to last quantifiable time ($AUMC_{0-24}$), area under the moment curve up to time infinity $AUMC_{0-\infty,}$ and the ratio $C_{max}/AUC_{0-\infty.}$

Statistical Analysis

Pharmacokinetic data was statistically been analyzed by using paired *t*-test. Comparison of pharmacokinetic parameter $C_{max,}$ AUC_{0-24}, $AUC_{0-\infty}$ and ratio for untransformed and ln- transformed data with respect to test and reference formulations analyzed using ANOVA (Dublin, Ireland). This analysis reflected the significance of various effects such as period, sequence, and subject tested within sequence. The predetermined equivalence range of 80-125% and $p \leq 0.05$ for the 90% CIs according to the guidelines of the USFDA were the basis of bioequivalence confirmation.

Results

Under the analytical conditions, the retention time of omeperazole and pantoprazole were 5.44 and 3.67 min respectively. No interfering peaks observed at corresponding retention time. A linear relationship ($r^2 = 0.9972$) was obtained in the calibration curve constructed over a range of 0.0-200 ng/mL. Coefficient of variation was always lower than 8%. The method had a precision of 96.99 ± 4.89 % and its limit of detection was 5.0 ng/mL.

Pharmacokinetic parameter

Pharmacokinetic parameters calculated from plasma drug level at defined time points for both reference and test products tabulated in Table 1. For reference and test products, the mean (SD) values of pharmacokinetic parameters were C_{max}; 345.28 and 316.23 ng/ml, t_{max}; 2.28 and 2.69 h, $t_{1/2}$; 2.57 and 2.39 h , AUC_{0-24}; 710.01 and 771.13 h-ng/mL, $AUC_{0-\infty}$; 848.21 and 902.56 h-ng/ml, MRT; 4.25 and 4.38 h, $AUMC_{0-24}$;174.51 and 192.56 h^2ng/ml, $AUMC_{0-\infty}$; 195.28 and 215.254 h^2ng/ml, k_{el}; 0.269 and 0.289 respectively. The Least Square Mean (LSM) ratios (%) in 90% CI of the ln-transformed values were 81.634 – 102.211% for C_{max}, 89.245 – 103.154% for $AUC_{0–24}$, and 86.264 – 104.218% for $AUC_{0–\infty}$ (Table 2). On the basis of the pharmacokinetic parameters, the

relative bioavailability of the generic test preparation Proceptin 20mg Capsule is 108.61 % to that of reference formulation Losec 20mg MUPS Tablet.

Mean plasma-concentration-against-time curves of two oral pharmaceutical formulations: Losec® and Proceptin® viewed in Figure 1 exhibited a similar kinetics. Inter-individual variability in omeperazole plasma concentrations was small. Subject variation was evidenced at 10 percent significant level for C_{max} ($p<0.01$), AUC_{0-24} ($p<0.01$), $AUC_{0-\infty}$ ($p<0.01$), $AUMC_{0-24}$ ($p<0.01$) and $AUMC_{0-\infty}$ ($p<0.01$) but no variation regarding formulation, period and sequences aspect showed in Table 3. For all subjects, there was a very fast absorption, a peak concentration of about 345.28 and 316.23 ng/ml being attained at 2.28 and 2.69 h for reference and test formulation respectively. The half-life of the reference and test products was also 2.57 h and 2.39 h respectively. No statistically significant differences observed in pharmacokinetic parameters when both formulations compared by paired *t*-test depicted in Table 4.

Discussion

Two striking observations regarding high variability between individuals and substantial differences between the two formulations within each individual are the significant consideration in any comparative pharmacokinetics study. Considerable inter-individual variability, particularly in C_{max}, AUC, and AUMC depicted for both formulations of omeperazole. This variability can be largely attributed to genetic polymorphism of the cytochrome P450 (CYP) isoform CYP2C19. [21-23] Besides age, concomitant medication and differences in weight could add to the high inter-individual variability.

In order to establish bioequivalence of two formulations tested, pharmacokinetic parameters for both test and reference preparations were compared by analysis of variance, and no statistically significant difference was observed. Moreover, ratios and 90% confidence limits for AUC_{0-24} and C_{max} were calculated. Confidence limits 89.54 (81.634 – 102.211%) for C_{max}, 104.34 (89.245 – 103.154%) for $AUC_{0–24}$ were within the limits of acceptance, which justified bioequivalence standard (Table 2). These limits of acceptance were selected based on the variability of omeperazole pharmacokinetics and double peaks or major shouldering characteristics. [14-18] It has been proposed that, in case of drugs with a wide variability in absorption, these limits are adequate [24,25] and are currently accepted in Europe.

From the results it was observed that the relative bioavailability of the generic test preparation Proceptin 20mg Capsule is 108.61 % equivalent to that of reference formulation Losec 20mg MUPS Tablet. This result confirmed the predetermined equivalence range of 80-125% with $p \leq 0.05$ for the 90% CIs according to the guidelines of the USFDA.

From a comparison perspective, pharmacokinetic parameters of omeperazole obtained in Bengali healthy subjects are not completely in accordance with data reported in the literature. Racial and ethnic variations in drug pharmacokinetics have no exception. As a fact of precedence, Poo *et al* [2] have reported that omeperazole capsules 20 mg orally administered to 34 healthy Mexican volunteers produced mean reference verses test in AUC_{0-t}, C_{max}, T_{max}, and $t_{1/2}$ values of 0.88 and 0.92 µg.h/ml, 0.49 and 0.48 µg/ml, 1.9 and 2.0 h, 0.85 and 0.91 h respectively. Allegrini *et al* [26] have found that omeperazole 20 mg capsules in 50 healthy Italian male and female volunteers produced a mean reference verses test preparations of AUC_{0-t} 908.95 and 900.83 ng.h/ml, C_{max} 447.61 and 436.31 ng/ml, T_{max} 2 and 2 h, and $t_{½}$ 1.27 and 1.06 h respectively. Rhim *et al* [27] studied with omeperazole 20 mg administering in healthy Korean male volunteers and reported a mean reference verses test preparation of AUC_{0-24} of 1223.3 and 1284.3 ng.h/ml, C_{max} of 598.7 and 598.1 ng/ml, T_{max} of 1.9 and 1.9 h, and $t_{1/2}$ of 1.3 and 1.4 h respectively. However, in the present study, mean test verse reference preparations of AUC_{0-24} was 771.13 and 710.01 ng.h/ml, C_{max} was 316.23 and 345.28 ng/ml, T_{max} was 2.69 and 2.28 h, and $t_{1/2}$ was 2.39 and 2.57 h respectively. In this study the lowest C_{max} and comparatively higher T_{max} and $t_{1/2}$ values were observed in Bengali population in comparison to Mexican, Italian and Korean subjects. These differences may be due to especially for CYP2C19 and CYP3A4 genotypes [21-23] and may be due to two different formulations considered in the comparative study. Single dose design and young healthy volunteer selection are main cruxes of limitation of this study as pharmacokinetics in patients may not be similar.

Conclusion

The results of the study stipulated that, the test and reference formulations of omeperazole meet the regulatory criteria for bioequivalence. On the basis of the pharmacokinetic parameters studied among the two formulations, it can be concluded that the test preparations Proceptin 20mg capsule was bioequivalent to the reference product Losec 20 mg MUPS tablet and can be substituted.

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Declarations of interest

The authors declare that there is no conflict of interest.

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Table 1 Plasma pharmacokinetic parameters of all the volunteers for test and reference formulations.

Reference formulation					
Pharmacokinetic parameters	Mean ± SD[a]	Geometric Mean	CV (%)[b]	Max	Min
C_{max} (ng/ml)	345.28 ± 42.38	335.46	25.35	378.43	197.54
t_{max} (h)	2.28 ± 0.16	2.19	34.56	2.56	1.9
AUC_{o-24}(h. ng/ml)	710.01± 92.51	702.56	43.46	805.58	596.63
$AUC_{o-\infty}$(h.ng/ml)	848.21± 65.31	835.23	38.54	942.51	605.74
MRT(h)	4.25 ± 0.342	4.04	23.45	4.83	3.88
$AUMC_{o-24}$ (h^2ng/ml)	174.51 ± 0.04	170.56	35.33	187.44	130.02
$AUMC_{o-\infty}$(h^2ng/ml)	195.28 ± 0.06	189.47	32.67	257.46	134.53
K_{el}	0.269 ± 0.04	0.226	25.46	0.299	0.185
$t_{1/2}$ (h)	2.57 ± 0.53	2.35	26.34	2.99	2.25
$C_{max}/AUC_{o-\infty}$	0.407 ± 0.03	0.387	35.77	0.463	0.346
Test formulation					
C_{max} (ng/ml)	316.23 ± 26.12	310.48	28.46	369.63	185.04
t_{max} (h)	2.69 ± 0.23	2.37	33.54	2.97	1.83
AUC_{o-24}(h. ng/ml)	771.13 ± 102.35	763.42	42.76	825.82	584.33
$AUC_{o-\infty}$(h.ng/ml)	902.56 ± 45.23	897.49	41.35	942.51	605.25
MRT(h)	4.38 ± 0.257	4.24	36.66	5.12	3.57
$AUMC_{o-24}$ (h^2ng/ml)	192.56 ± 0. 02	185.38	40.32	237.65	140.58
$AUMC_{o-\infty}$(h^2ng/ml)	215.25 ±0.13	205.56	43.57	266.49	154.66
K_{el}	0.289 ± 0.08	0.235	29.57	0.332	0.164
$t_{1/2}$ (h)	2.39 ± 0.79	2.14	34.43	3.24	2.16
$C_{max}/AUC_{o-\infty}$	0.350 ± 0.21	0.281	37.66	0.384	0.314

[a]SD=Standard Deviation, [b]CV=Coefficient of Variance

Table 2. The 90% confidence Interval with the Test and Reference Preparation

Parameter	Untransformed data	ln transformed data
C_{max}	0.88645 – 1.10241%	0.81634 – 1.02211%
AUC_{0-24}	0.86230 – 1.22654%	0.89245 – 1.03154%
$AUC_{0-\infty}$	0.85056 – 1.02598%	0.86264 – 1.04218%

Table 3. The *p* values for sources of variations obtained from Analysis of Variance (ANOVA).

Pharmacokinetic parameters	Sources of variation			
	Formulation	Period	Sequence	Subject
C_{max} (ng/ml)	0.12	0.77	0.66	0.01
t_{max} (h)	0.77	0.57	0.84	0.06
AUC_{0-24}(h.ng/ml)	0.84	0.78	0.66	0.01
$AUC_{0-\infty}$(h.ng/ml)	0.64	0.89	0.75	0.01
MRT(h)	0.85	0.56	0.83	0.26
$AUMC_{0-24}$ (h^2ng/ml)	0.96	0.77	0.52	0.01
$AUMC_{0-\infty}$(h^2ng/ml)	0.93	0.65	0.72	0.01
K_{el}	0.74	0.84	0.61	0.17
$t_{1/2}$ (h)	0.86	0.72	0.84	0.15

Table 4. The *p* values of paired t-test.

Pharmacokinetic parameters	p values
C_{max} (ng/ml)	0.257
t_{max} (h)	0.657
AUC_{0-24}(h.ng/ml)	0.879
$AUC_{0-\infty}$(h.ng/ml)	0.856
MRT(h)	0.763
$AUMC_{0-24}$ (h^2ng/ml)	0.451
$AUMC_{0-\infty}$(h^2ng/ml)	0.485
K_{el}	0.64
$t_{1/2}$ (h)	0.359

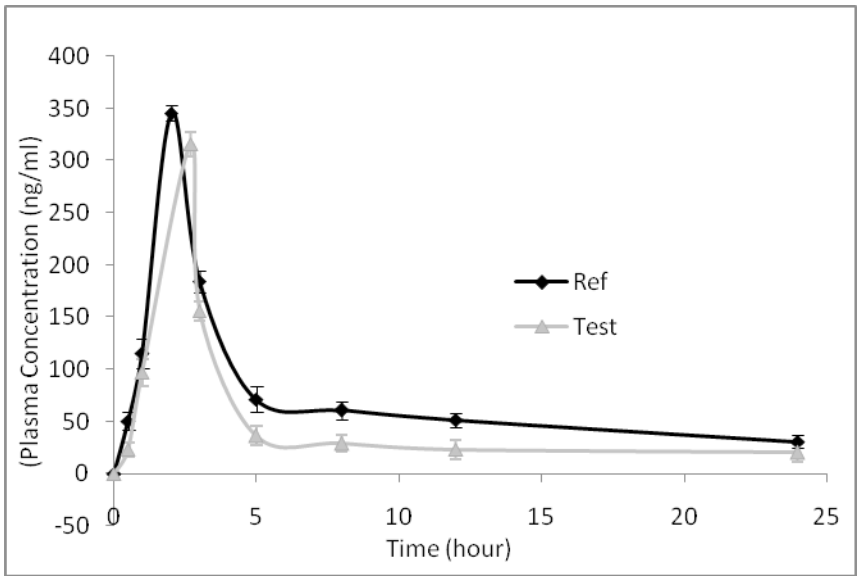

Figure 1. Mean plasma-concentration-time curve of omeprazole after oral administration of two formulations: Reference (Losec®) and Test (Proceptin®) products to healthy subjects.

ADVERSE DRUG REACTION : A LEADING CAUSE OF DEATH WORLDWIDE

Dr. Muniruddin Ahmed

In medical science, an adverse drug effect is defined as a harmful and undesired effect resulting from a medication or other intervention such as chemotherapy and surgery. Sometimes an adverse effect may be termed a 'side-effect' and may result from an unsuitable or incorrect dosage or procedure which may result from medical error. Adverse effects are sometimes referred to as Iatrogenic because they are generated by a physician and his or her treatment. Using a drug or other medical intervention which is contraindicated may increase the risk of adverse effects to a great extent. Adverse effects may cause serious complications of a disease or procedure and negatively affect its prognosis. The harmful outcome is usually indicated by some result such as morbidity, mortality, change in body weight, levels of enzymes, loss of function, or as a pathological change detected at the microscopic, macroscopic or physiological level. It may also be indicated by symptoms reported by a patient. Adverse effects may cause a reversible or irreversible damage, including an increase or decrease in the susceptibility of the individual to other chemicals, foods or procedures like drug interaction.

Some of the adverse drug reactions (ADR) are so serious that these may cause death, hospitalization, or serious injury to millions of people around the world each year, including millions of fatalities. In fact, adverse drug reactions are one of the leading causes of death in the world. It may seem unbelievable that in most cases and most of the time, these dangerous side effects or adverse effects could and should have been avoided. Most of the people around the world do not know that even simple unwanted reactions, such as change in mood, loss of appetite, nausea and vomiting may seriously diminish the quality of life.

According to the recent statistics more adverse reactions occur in patients of 60 years or older, but the suffering of an adverse drug reaction may begin to increase even before the age of 50. Almost 50 percent reports of the Food and Drug Administration (FDA) of deaths from adverse drug reactions and 61 percent of hospitalizations from adverse drug reactions were in people younger than 60. Many physical changes that affect the way the

body can handle drugs actually begin in people in their thirties, but the increased prescribing of drugs does not begin for most people until they enter their fifties. By then, the amount of prescription drug use starts increasing significantly, and therefore the odds of having an adverse drug reaction also increase. The risk of an adverse drug reaction is about 33percent higher in people aged 50 to 59 than it is in people aged 40 to 49.

An analysis of numerous studies in which the cause of hospitalization was determined found that approximately 1.5 million hospitalizations a year were caused by adverse drug reactions. This means that every day more than 4,000 patients have adverse drug reactions so serious that they need to be admitted to American hospitals. A review of patients admitted to medical wards of a hospital found that although for 3.8 percent of hospital admissions, adverse drug reactions led directly to hospitalization, 57 percent of these adverse drug reactions were not recognized by the attending physician at the time of admission. As in numerous other studies, many of these admissions should have been prevented. In fact, 18.6 percent of all drugs prescribed prior to admission were contraindicated.

Another review of studies of the percentage of hospital admissions related to adverse drug reactions found that up to 88 percent of ADR-related hospitalizations in the elderly are preventable. In addition, elderly people were four times more likely to be hospitalized by ADR-related problems than nonelderly.

Although the rate of drug-induced hospitalization is higher in older adults because they use more drugs, a significant proportion of hospitalizations for children are also caused by adverse drug reactions. A recent review of all studies concerning the reasons for pediatric hospitalization of children under the age of 19 found that 2.09 percent of all pediatric hospitalizations were caused by adverse drug reactions and that 39 percent of these were life-threatening. Using the most recent published data on pediatric hospitalizations, there were 3.8 million children under the age of 19 hospitalized in the United States in 1997. This means that in one year, there are 79,000 children admitted to the hospital because of adverse drug reactions, 31,000 of these children having life-threatening adverse reactions. A recent review of studies concerning the causes of people going to hospital emergency rooms found that as many as 28 percent of all emergency department visits were drug-related, including a large proportion due to adverse drug reactions and inappropriate prescriptions. Of all of the drug-related visits, the authors found that 70 percent were preventable.

In addition to the 1.5 million people who are admitted to the hospital because of adverse drug reactions, additional three-quarters of a million people a year develop an adverse reaction after they are hospitalized. According to national projections based on a study involving adverse drug reactions developing in patients in the hospital, 770,000 additional patients a year—more than 2,000 patients a day—suffer an adverse event caused by drugs once they are admitted. Many of the reactions in the patients studied were serious, even life-threatening, and included cardiac arrhythmias, kidney failure, bleeding, and dangerously low blood pressure. People with these adverse reactions had an almost twofold higher risk of death compared to other otherwise comparable hospitalized patients who did not have a drug reaction. Most important, according to the researchers, almost 50 percent of these adverse reactions were preventable. Among the kinds of preventable problems were adverse interactions between drugs that should not have been prescribed together, known allergies to drugs that had not been asked about before the patients got a prescription, and excessively high doses of drugs prescribed without considering the patient's weight and kidney function.

Thus, adding the number of people with adverse drug reactions so serious that they require hospitalization to those in which the adverse reaction was 'caused' by the hospitalization, more than 2.2 million people a year, or 6,000 patients a day, suffer these adverse reactions. In both situations, many of these drug-induced problems should have been prevented.

Adverse drug reactions cost approximately $136 billion annually, which is more than the total costs of cardiovascular and diabetic care, according to a study on drug-related morbidity and mortality, according to a study published in the Journal of the American Pharmacists Association. There are 106,000 deaths each year due to adverse drug reactions, ranking it anywhere from fourth to sixth among the leading causes of death, according to the study "Adverse Drug Reactions in United States Hospitals." Among hospitalized patients, adverse drug reactions cause one out of every five injuries or deaths per year, according to a Harvard Medical Practice study

Adverse effects can occur as a collateral or side effect of many interventions, but they are particularly important in pharmacology, due to its wider and sometimes uncontrollable use by way of self medication. Thus, reasonable drug use becomes an important issue here.

Adverse effects, like intended effects of drugs, are a function of dosage or drug levels at the target organs, so they may be avoided or decreased by means of careful and precise pharmacokinetics (the change of drug levels in the organism in function of time after administration). Adverse effects may also be caused by drug interaction i.e., when physicians fail to check for all medicaments a patient is taking and prescribe new ones which interact agonistically or antagonistically (potentiate or decrease the intended therapeutic effect). Significant morbidity and mortality is caused around the world because of this. Drug-drug and food-drug interactions may occur, and even so-called 'natural drugs' used in alternative medicine may have dangerous adverse effects. For example, extracts of St. John's wort, a herbal product used for treating mild depression are known to cause an increase in the cytochrome P450 enzymes responsible for the metabolism and elimination of many drugs, so that patients taking it are likely to experience a reduction in blood levels of drugs that they are taking for other purposes, such as cancer chemotherapeutic drugs, protease inhibitors for HIV and hormonal contraceptives. The scientific field of activity associated with drug safety is increasingly government-regulated and is of major concern for the public as well as to drug manufacturers. Imperfections in clinical trials, such as insufficient number of patients or short duration, sometimes lead to public health disasters such as those of fenfluramine -an antiobesity medication which consisted of two drugs: fenfluramine and phentermine. Fenfluramine, and later, a related drug, dexfenfluramine, were marketed by American Home Products, now known as Wyeth. After reports of valvular heart disease and pulmonary hypertension, primarily in women who had been undergoing treatment with fenfluramine, the Food and Drug Administration requested its withdrawal from the market in September 1997. The action was based on findings from doctors who had evaluated patients taking these two drugs with echocardiograms, a special procedure that can test the functioning of heart valves. These findings indicated that approximately 30 percent of patients who were evaluated had abnormal echocardiograms, even though they had no symptoms. This percentage of abnormal test results was much higher than would be expected from a comparatively-sized sample of the population who had not been exposed to either fenfluramine or dexfenfluramine. In July 1997, researchers at the Mayo Clinic and Mayo Foundation reported 24 cases of rare valvular disease in women who took the fenfluramine combination therapy. The FDA alerted medical doctors that it had received nine additional reports of the same type, and requested all health care professionals to report any such cases to the agency's MedWatch program, or to their respective pharmaceutical manufacturers.

The FDA subsequently received 66 additional reports of heart valve disease, all primarily associated with fenfluramine. There were also reports of documented heart-valve problems in patients taking only either fenfluramine or dexfenfluramine. The FDA requested that the manufacturers of fenfluramine and dexfenfluramine stress the potential risk to the heart in the drugs' labeling and in patient package inserts. As of 1997, the FDA was continuing to receive reports of cardiac valvular disease in persons who have taken these drugs. This valvular disease typically involves the aortic and mitral valves. As of 2004, fenfluramine is no longer widely available. In April 2005, *American Lawyer* magazine ran a cover story on the fenfluramine mass tort crisis, reporting that more than 50,000 product liability lawsuits had been filed by alleged fenfluramine victims. Estimates of total liability run as high as $14 billion. Thalidomide is a sedative, hypnotic, and multiple myeloma medication. The drug is a potent teratogen in rats, rabbits, non-human primates and humans. Thalidomide was developed by German pharmaceutical company Grünenthal. It was sold from 1957 to 1961 in almost 50 countries under at least 40 names, including Distaval, Talimol, Nibrol, Sedimide, Quietoplex, Contergan, Neurosedyn, and Softenon. Thalidomide was chiefly sold and prescribed during the late 1950s and early 1960s to pregnant women, as an antiemetic to combat morning sickness and as an aid to help them sleep. Before its release inadequate tests were performed to assess the drug's safety, with catastrophic results for the children of women who had taken thalidomide during their pregnancies. From 1956 to 1962, approximately 10,000 children were born with severe malformities, including phocomelia (an extremely rare congenital disorder involving malformation of the limbs), because their mothers had taken thalidomide during pregnancy. In 1962, in reaction to the tragedy, the United States Congress enacted laws requiring tests for safety during pregnancy before a drug can receive approval for sale in the U.S. Other countries enacted similar legislation, and thalidomide was not prescribed or sold for decades.

Researchers, however, continued to work with the drug. Soon after its banishment, a doctor discovered anti-inflammatory effects of thalidomide and began to look for uses of the medication despite its teratogenic effects. They found that patients with erythema nodosum leprosum, a painful skin condition associated with leprosy, experienced relief of their pain by taking thalidomide. Further work showed that it was effective in multiple myeloma, and it is now approved by the FDA for use in this malignancy. There are studies underway to determine the drug's effects on arachnoiditis, Crohn's disease, and several types of cancers. However, physicians and

patients alike must go through a special process to prescribe and receive thalidomide to ensure no more children are born with birth defects traceable to the medication. The withdrawal of cerivastatin from the world market in 2001 generated substantial attention in the media. Cerivastatin is a synthetic member of the class of statins, used to lower cholesterol and prevent cardiovascular disease. It was withdrawn from the market because of the high rate of serious side-effects. Cerivastatin was marketed by the pharmaceutical company Bayer A.G. in the late 1990s as a new synthetic statin, to compete with Pfizer's highly successful Lipitor. During post-marketing surveillance, 52 deaths were reported in patients using cerivastatin, mainly from rhabdomyolysis and its resultant renal failure. Risks were higher in patients using fibrates and in patients using the high dose of cerivastatin. Another 385 nonfatal cases of rhabdomyolysis were reported. This put the risk of this complication at 5-10 times that of the other statins. On August 8, 2001 the U.S. Food and Drug Administration (FDA) announced that Bayer Pharmaceutical Division voluntarily withdrew Baycol from the U.S. market, due to reports of fatal Rhabdomyolysis, a severe adverse reaction from this cholesterol-lowering (lipid-lowering) product.

Rofecoxib is a nonsteroidal anti-inflammatory drug (NSAID) developed by Merck to treat osteoarthritis, acute pain conditions, and dysmenorrhoea. Rofecoxib was approved as safe and effective drug by the Food and Drug Administration (FDA) on May 20, 1999 and was subsequently marketed under the brand name Vioxx, Ceoxx and Ceeoxx. Rofecoxib gained widespread acceptance among physicians treating patients with arthritis and other conditions causing chronic or acute pain. Worldwide, over 80 million people were prescribed rofecoxib at some time. On September 30, 2004, Merck voluntarily withdrew rofecoxib from the market because of concerns about increased risk of heart attack and stroke associated with long-term, high-dosage use of the drug. Rofecoxib was one of the most widely used drugs ever to be withdrawn from the market. In the year before withdrawal, Merck had sales revenue of US$2.5 billion from Vioxx.

At the conclusion I would like to present some of the most prominent adverse effect of drugs. These are: Abortion, miscarriage or uterine hemorrhage associated with misoprostol- a labor-inducing drug (this is a case where the adverse effect has been used legally and illegally for performing abortions), Addiction to many sedatives and analgesics such as diazepam, morphine, Bleeding of the intestine associated with aspirin therapy Deafness and kidney failure associated with gentamicin (an antibiotic) Death, following sedation in children using propofol, Dementia associated with heart bypass surgery, Depression or hepatic injury caused by interferon, Diabetes caused

by atypical antipsychotic medications (neuroleptic psychiatric drugs), Diarrhea caused by the use of orlistat, Erectile dysfunction associated with many drugs, such as antidepressants, Fever associated with vaccination (in the past, imperfectly manufactured vaccines, such as BCG and poliomyelitis, have caused the very disease they intended to fight), Glaucoma associated with corticosteroid-based eye drops, Hair loss and anemia may be caused by chemotherapy against cancer, leukemia, etc., Headache following spinal anesthesia, Hypertension in ephedrine users, which prompted FDA to remove the status of dietary supplement of ephedra extracts, Insomnia caused by stimulants, Lactic acidosis associated with the use of stavudine for anti-HIV therapy) or metformin (for diabetes), Melasma and thrombosis associated with use of estrogen-containing hormonal contraception such as the combined oral contraceptive pill, Rhabdomyolysis associated with statins (anti-cholesterol drugs), Seizures caused by withdrawal from benzodiazepine, Sleepiness or increase in appetite due to antihistamine use, Stroke or heart attack associated with sildenafil when used with nitroglycerine, Suicide, increased tendency associated to the use of fluoxetine and other SSRI antidepressants, Tardive dyskinesia associated with long-term use of metoclopramide and many antipsychotic medications.

Some advices from a pharmacist to get rid of adverse drug reactions:

1. Everybody should remember that there is no pill for every ill. We do not even need pills for every ill. Try to remain healthy without medicines, if possible.
2. There is a proverb in medical sciences. It goes like this- ‘All medicines are poisons. There is none which is not a poison. Only the right dose differentiates the remedy and the poison.’
3. Self medication may be sometimes dangerous. Consult your physicians before taking drugs.
4. Ask the physician about the possible side effects or drug interactions of the drugs which have been prescribed for you
5. If you suffer from the adverse drug reaction or side effects after taking drug(s), immediately stop taking the drug and consult your physician

6. If you think you may have penicillin allergy, talk to your doctor about getting an allergy skin test. Research has shown that penicillin or other antibiotic allergies may be over reported. Ruling out an antibiotic allergy can help your doctor prescribe the most appropriate antibiotic when it's needed.

7. Antibiotics have potential adverse effects. Do not misuse antibiotics. Use antibiotics only as prescribed by your doctor. If you have an antibiotic prescription, ask your doctor what could be the possible side effects of the drug.

8. Pay attention to side effects**.** Don't dismiss changes in your health or behavior. These could be signs of an adverse reaction. Also listen to your friends and family members who may notice changes before you do.

9. Take the right medication at right doses for right times as per the prescription of your physician**.** One of the biggest causes of adverse drug interactions is taking too much or too little of your prescribed drugs.

10. Herbal drugs may have potential side effects. Do not take any kind of herbal drugs without being sure of its efficacy and safety. Do not believe the highly motivated statement -"Herbal drugs have no side effects."

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PREVENTION AND REVERSAL OF CORONARY ARTERY DISEASE (CAD)

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The heart is supplied by oxygen and nutrients via the coronary arteries. There are significant consequences when the heart does not receive the necessary amount of blood. This issue is exacerbated through plaque formation, which causes the arteries to become narrower as we age. Is there anything that we can do to slow down this process or to potentially reverse it? Research studies indicate that we can implement several measures to minimize the risk of total or significant coronary blockages which may later require medical or surgical intervention. There are several risk factors associated with coronary blockages:

1. Genetics
2. Aging
3. Prediabetes and Diabetes
4. Smoking
5. Stress
6. High blood pressure
7. High LDL with very low particle size
8. Low HDL
9. High homocysteine level
10. High C reactive protein level
11. Low Vitamin D level
12. Food and Lifestyle
13. Weight gain
14. Belly fat and waist circumference

1. Genetics

Although we cannot change our genes, it is very possible to influence the expression of our genes with lifestyle changes, diet, and the use of certain nutritional supplements.

2. Aging

We cannot stop the aging process, however we can influence chronic inflammation and oxidation in order to minimize plaque deposit and atherosclerosis.

3. Prediabetes and Diabetes

A person is considered to be pre-diabetic when the fasting blood sugar level is between 100 mg/dl to 125 mg/dl or the HbA1c level is between 5.7% to 6.4%. A person is also considered pre-diabetic if the oral glucose tolerance test (OGTT) is between 140 mg/dl to 199 mg/dl. A person is considered diabetic if fasting blood sugar level is 126 mg/dl or higher or if the HbA1c level is 6.5% or higher. A person with an OGTT over 200 mg/dl is also considered to be diabetic.

Anytime our fasting blood sugar level is over 100 mg/dl, our risk of developing CAD continues to rise proportionately with the increase in blood sugar level. Since increases in blood sugar level also increase the blood lipid level and the oxidation of LDL cholesterol, our risk of developing CAD increases with higher blood sugar level. The best way to manage diabetes and prediabetes is through proper dietary changes, exercise and taking certain supplements. Although medication reduces the blood sugar level artificially, it is not addressing the core issue of insulin resistance. For Type 2 diabetes management, using insulin as a treatment can be problematic since high amounts of free insulin level in the blood may increase the risk of weight gain and plaque formation.

4. Smoking

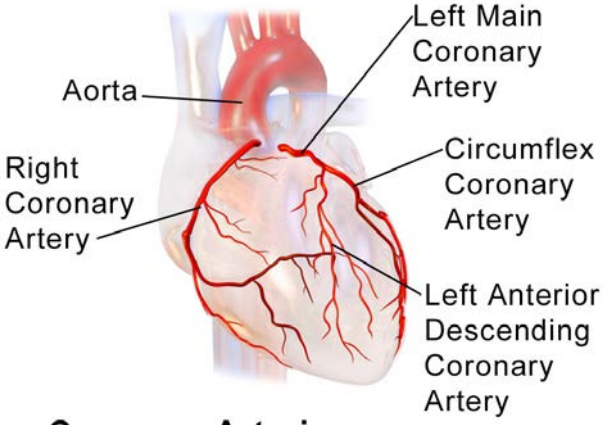
Smoking in general increases the risk of coronary heart disease. Smoking damages the lining of the blood vessels, which promotes the build-up of fatty materials and plaque formation.

5. Stress

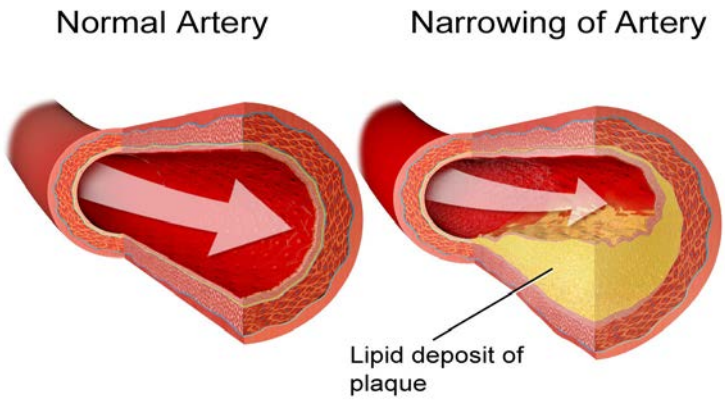
We all experience stress for one reason or another. During stressful situations, our body produces cortisol and adrenaline. Adrenaline constricts the blood vessels, which in turn, increases blood pressure and causes damage to the blood vessels. In healthy people, cortisol peaks half an hour after awakening and continues to decline throughout the day, bottoming out around midnight. On the other hand, cortisol level remains high in those who are constantly stressed, which results in a perpetual feeling of tiredness. High cortisol level is now linked to atherosclerosis and plaque formation.

6. High Blood Pressure

Besides diabetes, high blood pressure can cause significant damage to the endothelium of blood vessels, which can influence buildup of cholesterol, other debris, and plaque formation. It is important to monitor blood pressure and keep it within normal limits. It is estimated that 50% of the US population will develop essential hypertension by age 60.



Coronary Arteries



Coronary Artery Disease

7. High LDL with very low particle size

Cholesterol in itself is not harmful. In fact, this is an essential fat. It provides stability to the cell membranes of our body's cells. We also need cholesterol to make the steroidal hormones and vitamins. Cholesterol is vital to normal brain function as well as the immune system. Twenty five percent (25%) of all the cholesterol

in our body is found in the brain. Cholesterol is the precursor for the formation of progesterone, estrogen, testosterone and vitamin D.

The total cholesterol level is not the most important parameter to gauge risk of atherosclerosis. An individual could have a total cholesterol level of 260 with very minimal risk of plaque build-up. On the other hand, a person with a total cholesterol level of just 150 can have significant risk of plaque build-up. Risk of atherosclerosis depends on the particle size, density, and risk of oxidation of the cholesterol particles. A special cholesterol test is required to determine the real risk of atherosclerosis.
This is called VAP cholesterol test.

8. Low HDL

High-density lipoprotein (HDL) plays an important role in atherosclerosis prevention. It is also known as good cholesterol since it helps transport low-density lipoprotein (LDL), triglycerides, fat molecules, macrophages etc. from inside the blood vessels to the liver for
elimination. Therefore, a healthy level of HDL is key to preventing CHD.

9. High homocysteine level

Homocysteine is a common amino acid and is derived mostly from eating meat. High homocysteine levels can damage the lining of the blood vessels which can lead to plaque formation. Therefore, it is advisable to minimize consumption of meat. Homocysteine levels can be reduced by taking B-vitamins and folic acid. It is reasonable to check homocysteine levels during yearly health screening.

10. High C-Reactive protein level

C-reactive protein (CRP) is mainly produced by the liver and increases in the presence of inflammation in the body. CRP levels usually rise if there is too much stress, exposure to environmental toxins, like smoking, secondhand smoking etc. Diet and lifestyle also have a huge impact to elevate CRP. Since chronic inflammation can damage the lining of the blood vessels, it is recommended that measures be taken to

reduce CRP levels. The normal range of CRP is 0 to 3. When CRP level exceeds 3, it signifies a high risk of developing CVD and heart disease. Lifestyle changes such as exercise, stress management and supplementing with Vitamin C and other antioxidants can help reduce CRP levels.

11. Low Vitamin D blood level

Our body makes most of the Vitamin D when a person gets enough exposure to the sun. However, in North America sun exposure is limited. Therefore, appropriate supplementation with Vitamin D3 is recommended. Many studies show that Vitamin D deficiency increases the risk of atherosclerosis, heart attack, congestive heart failure, stroke and CAD.

Normal 25-Hydroxy Vitamin D blood level ranges from 20 ng/ml to 50 ng/ml. However, most researchers recommend keeping vitamin D levels closer to 50 ng/ml. For cancer patients, it is recommended that vitamin D level be kept around 100 ng/ml.

12. Food and lifestyle

Food and lifestyle plays a major role in developing atherosclerosis and CAD. Overconsumption of carbohydrates (bread, pasta, rice) and refined sugars (sodas, cakes, candy) increases blood sugar level which promotes plaque formation. It is recommended to limit carbohydrate and refined sugar consumption as well as excessive saturated fats. A sedentary lifestyle also promotes chronic inflammation and CAD. The best foods to eat are: beans, greens, mushrooms, nuts, seeds, avocados, and berries.

13. Weight gain

Even a modest increase in weight can significantly increase the risk of atherosclerosis and heart disease. Weight gain almost always triggers insulin resistance and chronic inflammation. Both can promote atherosclerosis and plaque formation. It is important to adopt a lifestyle through which one can maintain the ideal body weight.

14. Belly fat and waist circumference

Recent research suggests that someone who has normal body

weight but a high waist to hip ratio is also at risk for heart disease and cardiovascular events.

Normal waist to hip ratios (WHR)

Males:		**Females:**	
Excellent	< 0.85	Excellent	< 0.75
Good	0.85 to 0.89	Good	0.75 to 0.79
Average	0.90 to 0.95	Average	0.80 to 0.86
At Risk	>= 0.96	At Risk	>= 0.87

To find out what your WHR is, first measure your waist and hip circumference and then calculate as shown below.

WHR = waist circumference / hip circumference

In summary, the best way to prevent atherosclerosis is to adopt an active lifestyle with good dietary habits and to take certain supplements.

Supplements that help prevent atherosclerosis:

Vitamin C (500mg - 1000mg / day) Preferably the powder form

Vitamin D3 as needed to keep blood level around 50 ng/ml

Grape seed extract (2 daily)

Pine bark extract (1 daily)

B-complex (1 tablet daily)

Fish oil (2 gm to 4 gm) daily

Coenzyme Q10 (200mg to 400mg) daily

Nattokinase (2 daily)

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