INTRODUCTION

The world of healthcare is not static, rather a dynamic one. Unprecedented developments in the pharmaceutical arena have offered a plethora of improvement and advancements in medicine and its dosage forms as well as new drug targets in the recent years. In addition, increasing life expectancy, acute and long-term conditions, and misuses of drugs leading to resistance and considerable risks of iatrogenic harm all place an increasing concern on the pharmaceutical companies. New molecules are being discovered and brought into the market. But do all the new drugs have justified clinical advantages over the existing ones? The objective of the study was to report on an investigation of a rather similar condition where diltiazem molecule has been found to be losing its market value in Bangladesh due to side effects and high price, resulting in the replacement by newer generations of the drug molecule. Diltiazem was generally indicated for the management of chronic stable angina and angina due to coronary artery spasm. One limitation of standard oral formulations has been found to be the need for multiple dosing on a daily basis. The sustained release (SR) form of the drug has been found to result in better compliance, reducing the frequency of dosage and in the end, the most important thing, maintaining a uniform drug concentration in the body. Transdermal delivery system of the drug can also be considered for the delivery of diltiazem HCL to achieve the effective plasma concentration for prolonged periods of time for the management of hypertension.

Keywords: Diltiazem HCL, sustained release, transdermal, patient compliance, Bangladesh
through the channel. The drug has medium vasodilation and a high degree of suppression of automaticity (SA node) and conduction (AV node). Safety in the drug treatment of hypertension can only be seen in relation to efficacy. Diltiazem has been also shown prospectively to reduce reinfarction following non-Q-wave Myocardial Infarction, a finding confirmed by a meta-analysis. Diltiazem has also been found to be associated with a very low rate of hypotension and to be effective in decreasing HR adequately in a prehospital setting. Pharmacokinetic features of Diltiazem HCL make it a potential candidate for extended release once-a-day dosage form. Diltiazem also prevents the tubular necrosis of kidneys through its calcium channel blocker action and maintains normal level of EPO which stimulates CFU cells in bone marrow for the production of hematopoietic cells. The radioprotective effect of diltiazem on Swiss albino mice exposed to gamma radiation was also studied and concluded that Diltiazem provides protection against radiation-induced haematological and biochemical alterations in Swiss albino mice.

![Figure 1: Structure of Diltiazem](image)

This calcium channel blocker works by relaxing blood vessels in the body and heart. It is used to control the heart rate in case of a fast/irregular heartbeat (atrial fibrillation). The SR forms of diltiazem have been found to be useful in treating high blood pressure. It has anti-anginal effect since it causes reduction in peripheral resistance and myocardial contractility. In addition, the dilatation of the peripheral vasculature reduces systemic pressure of cardiac ‘after load’ which results in lessened stress and reduced oxygen requirement of the myocardial tissues. The drug has been considered as the first line of treatment of prinzmetal variant angina and chronic stable angina pectoris. It also possesses antiarrhythmic properties due to its ability of inhibition of the influx of calcium ions in cardiac tissues that result in slow electrophysiological activity through the SA and AV nodes without affecting accessory bypass conduction or altering normal atrial action potential or intraventricular conduction. The absorption of these agents is nearly complete after oral administration and their bioavailability is reduced, owing to their vulnerability to first pass metabolism which is evident within the first 30-60 minutes of an oral dose. This makes the drug an ideal candidate for sustained release drug delivery. Many clinical data are available to prove these claims. It was found according to a study conducted by Boden et al in 2001, after the administration of diltiazem, multiple comparisons by baseline HR category showed a significant difference between both groups for baseline HR of 74-84 beats/min and > or = 85 beats/min (p = 0.001). Sustained-release diltiazem (at the usual clinical doses of 200 or 300 mg once daily) had no significant HR-decreasing effect on baseline HR 74 beats/min or less but appears to have a genuine regulating effect on HR: it reduces tachycardia without inducing excessive bradycardia. In another study by Frances et al, it was found that Diltiazem (200 and 300 mg) produced respectively a 68 % and a 64 % decrease in weekly angina episodes, and placebo a 15 % decrease (P < 0.05). Similarly, both dose levels produced a 70 % decrease in nitroglycerin consumption, whereas no difference was obtained with placebo (P < 0.01). The increase in time to ischemic threshold was significantly superior for 200 mg and 300 mg diltiazem when compared with placebo (75.2 and 91.5 sec respectively versus 47.0 sec) (P < 0.05); increase in time to angina threshold was also significantly greater for diltiazem when compared with placebo (84.6 and 85.9 sec respectively versus 43.9 sec) (P < 0.05).

**Objectives**

The principal objectives of the study are as follows:

- To analyse the market proportionality of diltiazem HCL in Bangladesh
- To find out the possibilities of the drug in sustained release delivery system
- To explore the improvement in the formulation in terms of manufacturing techniques and additives in order to give a comparative analysis and justification of proposed ideal formulations.

**Data**

The materials of the study are completely based on primary sources and secondary data obtained from different authentic sources that describe the dissolution studies of different materials on the modification of sustained release of the drug.

**Market Proportionality of Diltiazem HCL in Bangladesh**

The market of anti-hypertensive products for Bangladesh at the moment is BDT 1,040 crore with a growth of 13.5 %. In Bangladesh the patients with hypertension associated with bradycardia are nowadays prescribed dihydropyridines like amlodipine, nifedipine since the molecule works on the peripheral blood vessels for coronary hypertension. Calcium channel blocker (CCB)-related edema has been reported to be quite common in clinical practice. On the other hand, patients with hypertension associated with tachycardia are prescribed the non-dihydropyridines like diltiazem since they act directly on the heart. The market for DH in Bangladesh has slowly increased from a market growth rate of 4.48 % in 2009 to a growth rate of 11.17 % in 2013, after its inception 20 years ago. The products available in the market were analyzed and it was found that only 2 companies out of the 11 companies that are marketing this drug product contribute to 97 % of the total market share of the drug. In 2009, sales of Diltiazem HCL generated BDT 52.20 mn and in 2013 BDT 83.57 mn (Table 1). The product has seen a slow but strong annual growth in recent years, which shows that there is a market for this drug. Several companies have reported to shift to newer molecules such as amloidpine, nifadipine, etc, which are claimed by the physicians to be more effective than DH although several serious side effects are found with these drug molecules [primary source]. Approximately twenty physicians were surveyed regarding the prescribing of DH. Almost 65 % claimed that this drug was no doubt a good choice for reducing tachycardia, but there are better alternatives also considering the patient conditions in...
Sustained Release Drug Delivery

One limitation of standard oral formulations of calcium antagonists has been the need for multiple daily dosing. Sustained-release dosage forms that permit simpler regimens and a smoother therapeutic effect can be a solution to this limitation. Differences in drug pharmacokinetic and pharmacodynamic properties have led to development of several sustained-release delivery systems. This generally facilitates in the maintenance of uniform drug concentration in the body to maintain therapeutic efficacy. A suitable sustained release DH dosage form would not only enhance therapeutic efficacy and patient compliance but also produce more desirable blood drug levels and lower incidence of adverse effects\(^{18}\). Three major types of sustained release drug delivery are available: the osmotic pump, coated pellet, and slow-dissolving material released from a matrix. Each is currently utilized for specific calcium antagonists. The osmotic pump system with nifedipine (Procardia XL, Pfizer) allows once-daily dosing as well as improvements in certain side effects. Verapamil is available in formulations employing dissimilar release systems. The original sustained-action products (Calan SR, Searle; Isoptin SR, Knoll) utilize a matrix system; a subsequent product (Verelan; Lederle, Wyeth-Ayerst, A. H. Robins) utilizes timed-release pellets. Importantly, clinical efficacy appears to be maintained with these several drugs and formulations for their approved indications. Although a specific formulation may alter the absorption, metabolism, excretion, and blood levels of a drug, it does not alter basic drug properties. Thus, the major impact of sustained-release drug delivery system lies in potential compliance improvement and possible reduction of side effects related to serum drug profiles\(^ {18} \).

Pellets with Disintegrating Coatings

Lack of compliance to dosing regimens is widespread largely due to complicated regimens (e.g., too many medications, too frequent dosing) and swallowing difficulties. The sustained-release delivery system using pelletized, time-coated capsules has recently been revitalized. It is based on encapsulating several hundred microspherical pellets with a dissolvable capsule. With this system, the polymer coating of the drug pellet disintegrates when exposed to gastrointestinal fluids. The pellet coatings are of varying thicknesses in order to control drug release for less frequently. Diltiazem ideally uses this mechanism. Another coating technique consists of a multiparticulate bead system that will have multiple layers of drug, excipients, and release-controlling polymers called diffucaps. The beads may contain a layer of organic acid or alkaline buffer in order to control the solubility of a drug by creating an optimal pH microenvironment for drugs that are found to exhibit poor solubility in intestinal pH, in environments with pH greater than 8.0, or in physiological fluids. Diffucaps technology enables the development of once-daily controlled-release (CR) capsules or patient-compliant orally disintegrating tablet formulations (ODT – CR) comprising immediate-release (IR), sustained-release (SR), timed pulsatile-release (TPR) or timed sustained-release (TSR) bead populations multicoated with a weakly basic drug, an organic acid or an alkaline buffer, and a solid-solution and then further coated with one or more functional polymers (Figure 2)\(^ {18}\). Another option will be if the beads can contain a solid-solution of drug and crystallization inhibitor which will enhance bioavailability by maintaining the drug in its amorphous state.

Improvement of Diltiazem HCL in SR Dosage Form Formulation

The release pattern and kinetics of the drug in case of sustained release dosage form can be improved by the
Modification of the release pattern desirable as per the official monograph standard, such as the USP. This can be achieved by the addition of blend of different additives at different concentrations which results in the modification of the release pattern of the drug to have the desirable therapeutic effects of the drug in order to improve patient compliance.

**Polymer Modification**

When aqueous polyvinyl acetate dispersion (Kollicote SR 30D) composed of 27 % polyvinyl acetate (PVAc), 2.5 % povidone, 0.3 % sodium lauryl sulfate is used, it provides enormous flexibility, rendering the film-coated pellets compressible without rupture20.21. Kollicote SR 30D has, thereby, been demonstrated to effectively retard drug release from nonpareil based systems. However, selected plasticizer type and subsequent curing condition play important roles in controlling drug release from such a system22. Studies conducted by Jalil et al, 2008 found out that keeping all the other ingredients in the same ratio with the variation of the polymer concentration of Kollicote 30D, KSRD 15 and KSRD 20 containing 15 % and 20 % of the polymer showed a 29 % release at the first hours, 50 % release in 2.5 hours and 80 % release in 6 hours meeting the criteria for acceptable standards of the release pattern of sustained release formulation of Diltiazem HCL23. Studies conducted by Qazi F et al, 201324 showed that keeping all other formulation ingredients constant the case of modification of the concentration of hydroxypropylcellulose shows that 99 % drug release at 7 h by F-1 (20 % K4M) and at 15 h by F-9 (20 % K100M). The comparison shows that 99 % drug release at 12 h for F-3 and at 18 h for F-10 containing 30 % K4M and K100M respectively whereas drug release comparison of F-4 (40 % K4M) and F-11 (40 % K100M) shows a 99 % sustained drug release for 24 h. Again F-12 having a higher concentration of K100M released only 86 % over 24 h, however the same concentration released 99 % drug in 15 h.

**Modification of Coating Gum**

Addition of tamarind kernel polysaccharide obtained from the seed kernels of *Tamarindus indica* that belonging to the family Leguminosae, have been found improve properties such as viscosity, pH tolerance, noncarcinogenicity, mucoadhesive nature and biocompatibility. It is a branched polysaccharide with a main chain of β-1,4-linked glucopyranosyl units and a side chain consisting of single d-xylpyranosyl unit attached to every second, third and fourth d-locopyranosyl unit though an α-1,6 linkage. One d-galactopyranosyl unit is attached to one of the xylopyranosyl unit through a β-1,2-linkage25-26. The swelling profile index of tablet in phosphate buffer pH 7.4 after 8 hours found the tablet as eroded. The swelling index is directly proportional to the concentration of the tamarind xyloglucan. As the concentration of tamarind xyloglucan increases there is an increase in swelling index. The initial increase and subsequent decrease in swelling index was probably due to the erosion of the surface layer and the order of swelling was found out to 200 mg > 150 mg > 100 mg of the gum. In vitro dissolution studies a release of 85.84 ± 3, 92 to 99.62 ± 0.54 % within 24 hours of administration77. Another modification has been reported to be done with the use of Gum karaya and locust bean. Gum karaya, sometimes known as Sterculia gum is the dried exudates of the Sterculia urens tree. It is a complex polysaccharide of high molecular weight which on hydrolysis yield galactose, rhamnose and galacturonic acid. It occurs as partially acetylated derivatives and is compatible with other plant hydrocolloids as well as proteins and carbohydrates28-30. Locust bean gum (LB), also known as galactomamna, is obtained from the seed of Locust bean plant and is composed of a 1, 4-linked β-D mannan backbone with a 1, 6-linked α D-galactose side group. It is a non-ionic molecule consisting of 2000 residues; the ratio of mannose to galactose in the molecule is 4:132. The in-vitro dissolution studies showed the release of 13-26 % for khaya formulation but at the end of 12 h, the value rose to between 50-81 % indicating that the tablets extended release for more than 12 h. For matrix tablet formulated with KLB (Khaya and Locust Bean Gum) polymer blend in 1:1 ratio, the initial release in the 1st hour ranged from 18-83 %. At the end of 12 h, the figure was between 75 % and 98 %. On the other hand, the tablets containing the polymer blend K:LB:H (1:0:0.5:0.5) as the matrix showed a cumulative release of 53-92 % at the end of 12 hours. Previous studies have shown locust bean gum alone cannot efficiently control drug release. This study demonstrates that its combination with khaya gum is synergistic in controlling diltiazem release. Combination of khaya gum with HPMC led to even greater sustained than khaya gum or its combination with locust bean LB gum. Thus, a suitable combination of the two natural gums (khaya and locust bean gums may be successfully employed for formulating sustained-release matrix tablets of diltiazem33.

**Techniques**

**Floating Osmotic Drug Delivery System**

In terms of the techniques of drug delivery, several novel approaches have been developed. Floating Osmotic Drug Delivery System (FODDS) is one of the useful for achieving modified drug release pattern in upper GI tract. It consists of a table having osmotic core (containing drug, osmogent and excipients), an inner semi-permeable membrane (SPM), an outer gelling agent containing gas generating agent applied as compression coating and an orifice drilled through SPM for passage of drug. When this type of system comes in contact with gastric environment, carbon dioxide is generated by the breakage of the gelling agent, thus decreasing the density of tablet mass. As the density of tablet below 1 i.e. density of water, it becomes buoyant in GI fluid. At the same time, the osmotic core draws surrounding fluid across semi-permeable membrane by the osmotic pressure gradient mechanism and saturated solution of drug is formed. This pressure is relieved by the flow of saturated solution of drug through the delivery orifice34. Studies conducted by Mane et al, 2013, found out that drug formulated using the constant ratio of the active drug (90 mg), microcrystalline cellulose (150 mg), Talc (10 mg), Magnesium stearate (10 mg) with variation in the KCl, HPMC K4M and Lactose concentration to have a total weight of 350 mg in this mechanism showed a better release pattern which is less than the marketed formulation (Dilzem SR) is as follows (Table 2)35.

**Colonic Drug Delivery System**

The colon is attracting site of interest where poorly absorbed drug molecule may have an improved bioavailability. This region of the colon is recognized as having a somewhat less hostile environment with less diversity and intensity of activity than the stomach and small intestine with longer retention time facilitating the absorption of poorly soluble drugs. According to study conducted by Islam et al, 2010, this
system has been taken as a representative of colonic release tablet where dry blending of the active ingredient (Diltiazem HCL) with filler, lubricant and flow promoter is done followed by direct compression using the following formulations done. To investigate the effects of polymer and their content level on drug release eight formulations were prepared (Table 3)\textsuperscript{36}.  

Table 2: *In vitro* drug release through FODDS formulation (Mane et al, 2013)  

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>Formulation (Diltiazem SR)\textsuperscript{13,14}</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>10.84 ± 0.045</td>
<td>6.38 ± 0.046</td>
<td>12.3 ± 0.048</td>
<td>8.46 ± 0.056</td>
<td>11.56 ± 0.057</td>
<td>6.8 ± 0.058</td>
<td>9.38 ± 0.059</td>
<td>7.38 ± 0.060</td>
<td>8.465 ± 0.064</td>
</tr>
<tr>
<td>60</td>
<td>18.41 ± 0.050</td>
<td>8.68 ± 0.050</td>
<td>20.98 ± 0.052</td>
<td>17.11 ± 0.054</td>
<td>16.4 ± 0.055</td>
<td>15.27 ± 0.056</td>
<td>15.1 ± 0.057</td>
<td>12.89 ± 0.058</td>
<td>17.667 ± 0.059</td>
</tr>
<tr>
<td>120</td>
<td>25.47 ± 0.053</td>
<td>20.08 ± 0.055</td>
<td>27.87 ± 0.056</td>
<td>23.98 ± 0.057</td>
<td>21.98 ± 0.058</td>
<td>22.32 ± 0.059</td>
<td>25.89 ± 0.060</td>
<td>24.87 ± 0.061</td>
<td>24.906 ± 0.062</td>
</tr>
<tr>
<td>180</td>
<td>35.50 ± 0.053</td>
<td>26.78 ± 0.055</td>
<td>39.56 ± 0.056</td>
<td>36.02 ± 0.057</td>
<td>33.82 ± 0.058</td>
<td>35.26 ± 0.060</td>
<td>30.53 ± 0.061</td>
<td>28.67 ± 0.062</td>
<td>33.832 ± 0.063</td>
</tr>
<tr>
<td>240</td>
<td>45.40 ± 0.057</td>
<td>35.17 ± 0.060</td>
<td>48.38 ± 0.061</td>
<td>44.45 ± 0.062</td>
<td>42.06 ± 0.063</td>
<td>44.42 ± 0.064</td>
<td>39.67 ± 0.065</td>
<td>37.43 ± 0.066</td>
<td>43.571 ± 0.067</td>
</tr>
<tr>
<td>300</td>
<td>57.91 ± 0.057</td>
<td>45.07 ± 0.061</td>
<td>60.92 ± 0.062</td>
<td>56.97 ± 0.063</td>
<td>51.82 ± 0.064</td>
<td>60.41 ± 0.065</td>
<td>50.51 ± 0.066</td>
<td>47.34 ± 0.067</td>
<td>57.888 ± 0.068</td>
</tr>
<tr>
<td>360</td>
<td>65.84 ± 0.061</td>
<td>51.36 ± 0.062</td>
<td>74.8 ± 0.063</td>
<td>69.73 ± 0.064</td>
<td>63.64 ± 0.065</td>
<td>63.31 ± 0.066</td>
<td>61.04 ± 0.067</td>
<td>60.6 ± 0.068</td>
<td>63.332 ± 0.069</td>
</tr>
<tr>
<td>420</td>
<td>79.65 ± 0.064</td>
<td>69.03 ± 0.065</td>
<td>87.66 ± 0.066</td>
<td>82.2 ± 0.067</td>
<td>79.91 ± 0.068</td>
<td>79.77 ± 0.069</td>
<td>77.3 ± 0.070</td>
<td>71.37 ± 0.071</td>
<td>80.341 ± 0.072</td>
</tr>
<tr>
<td>480</td>
<td>92.33 ± 0.066</td>
<td>78.01 ± 0.067</td>
<td>98.21 ± 0.068</td>
<td>94 ± 0.069</td>
<td>89.91 ± 0.070</td>
<td>88.6 ± 0.071</td>
<td>84.58 ± 0.072</td>
<td>91.216 ± 0.073</td>
<td>95.21</td>
</tr>
</tbody>
</table>

Table 3: Formulations of Colonic release Diltiazem HCL tablets prepared by direct compression method  

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Formulation Code (mg/Tablet)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F-1</td>
</tr>
<tr>
<td>Diltiazem HCL</td>
<td>90</td>
</tr>
<tr>
<td>M K 4M Premium</td>
<td>55</td>
</tr>
<tr>
<td>M K 100 Premium CR</td>
<td>-</td>
</tr>
<tr>
<td>M K 15M CR</td>
<td>-</td>
</tr>
<tr>
<td>Xanthan Gum</td>
<td>-</td>
</tr>
<tr>
<td>Povidone (Kollidon 30)</td>
<td>10</td>
</tr>
<tr>
<td>Ludipress</td>
<td>100</td>
</tr>
<tr>
<td>Cross Carmelose Na</td>
<td>45</td>
</tr>
<tr>
<td>Na-Starch Glucolate</td>
<td>-</td>
</tr>
<tr>
<td>Kollidone CL (Crosspovidone)</td>
<td>-</td>
</tr>
<tr>
<td>Aerosil</td>
<td>3</td>
</tr>
<tr>
<td>Talc</td>
<td>2</td>
</tr>
<tr>
<td>Mg-Stearate</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>310</td>
</tr>
</tbody>
</table>

Diltiazem HCL. In F-8 Formulation, the release is only 73%. Diltiazem HCL tablet delivered drug at desired rate in the colon. The duration and extent of drug release of different formulations were different but fully in agreement with the USP specification. This experiment also indicates that the rate and extent of drug release could be modulated accordingly by varying amount of release modifier.  

Sintered Matrix Tablets  
The term sintering means fusion of particles or formation of welded bonds between particles of polymers. The sustained release oral dosage forms can also be developed by sintering the polymer matrix by exposing it to a temperature above the glass transition point of the polymer or exposing these matrix systems to solvent vapors. It has been shown by Shafi et al that DH is also a good candidate for sintered matrix tablets.  

Transdermal Delivery  
Transdermal drug delivery system of diltiazem hydrochloride using matrix diffusion controlled (MDC) and membrane permeation controlled (MPC) systems can be developed to obtain a prolonged controlled drug delivery\textsuperscript{37}. This drug delivery system of diltiazem HCL can be developed to deliver the drug so that a constant effective plasma drug concentration could be maintained for prolonged periods of time. Transdermal drug delivery system is a highly investigated drug delivery system of a number of drugs and many transdermal drug delivery systems of different drugs are commercialized\textsuperscript{38}. This method provides many advantages over conventional administration including enhanced efficacy, increased safety, greater convenience and improved patient compliance. This can avoid the “peak and valley” effect of oral or injectable therapy and can enable more controlled effective treatment by delivering drugs at a steady rate into bloodstream over an extended period of time. It also reduces the dosage-related side effects because the amount of drug delivered into the biological system in a very controlled manner and avoids first-pass metabolism\textsuperscript{39,40}. Various types of preparation and methods employed in the preparation of transdermal drug delivery systems are discussed in the literature\textsuperscript{41,42}.  

Page 687
Recommendation
Taking all the information given so far, the recommendation for an ideal sustained release formulation is as follows:
- Increasing the polymer concentration of Kollicoat 30D above 15% will increase the optimum release level of the drug.
- Increasing the HPMC polymer concentration should be above 40% will facilitate optimum drug delivery.
- Increasing the tamarind xyloglycan above 200 mg would help in the optimum dosage facilities.
- Increasing the concentration of the karaya gum and locust bean gum would increase the possibility of optimum drug delivery.
- A suitable sustained release diltiazem HCL dosage form would not only enhance therapeutic efficacy and patient compliance but also produce more desirable blood drug levels and lower incidence of adverse effects³.

In addition to the above, further investigations could be conducted on the novel techniques, e.g., Diffilac®, floated osmotic drug delivery system, sintered matrix release, transdermal delivery and colonic drug delivery system for the sustained release dosage forms of Diltiazem HCL. The possibility of the drug’s potentiality in comparison to the other drugs of the same therapeutic group may be then reconsidered. Finally, further studies could be conducted on the sales profile, release kinetics of marketed formulations as well as patient profile in Bangladesh in order to bring forward the merits and demerits of DH. Studies continue on this issue, and it is generally agreed that more evidence is needed⁴.

CONCLUSION
A vigorous debate continues about the relative merits of DH, particularly in treating high blood pressure. This is largely because a few studies indicate that CCBs (and particularly high doses taken over long periods) may be associated with a somewhat higher risk of heart attacks and heart failure compared to other medicines, such as diuretics, beta-blockers and ACE inhibitors. This does not mean that CCBs are causing heart attacks or heart failure because a few studies indicate that CCBs (and particularly high doses taken over long periods) may be associated with a somewhat higher risk of heart attacks and heart failure. Complications may arise but the parameters to facilitate in the development of diltiazem HCL may be considered so that the patients may be served in a better way as much as possible to improve the health profile of the cardiovascular patients in the country.

REFERENCES
16. Side effects of Diltiazem HCL. Drugs.com; 2104.
Kumar P, Singh S, Mishra B. Floating osmotic drug delivery system of
Gupta BP, Thakur N, Jain NP, Banweer J, Jain S. Osmotically
controlled Drug Delivery System with Associated Drugs. J Pharm

Moin A and Shivakumar HG. Formulation of Sustained-Release
Diltiazem Matrix Tablet Using Hydrophilic Gum Blends. Trop J Pharm

Mae SS, Kamble MG, Mane OR, Borwandkar VG, Aute PP, Chaudari
PD, Bhosale AV. Optimization of Floating Osmotic Drug Delivery
System of Diltiazem Hydrochloride Using 3 Factorial Design. Indo Am

Islam MS, Chowdhury JA, Tania SM. Study on the Development of
Diltiazem HCL Loaded Colonic Drug Delivery Systems (CDDS) Using
Various Polymers and Characterization of their Release Profile by In

Shaif S, Chowdary KA, Shivappa N, Sachin H. Formulation and
Evaluation of Sintered Matrix Tablets of Diltiazem Hydrochloride.

Jain SK, Chourasria MK, Sabitha M, Jain R, Jain AK and Ashawat M.
Development and Characterization of Transdermal Drug Delivery
177. http://dx.doi.org/10.1080/713840400

Ranade VV. Drug delivery systems. 6. Transdermal drug delivery. J.
4604.1991.tb01881.x

Cite this article as:
Eva Rahman Kabir, Samin Huq. Diltiazem HCL: Evaluation of it’s presence
in Bangladesh. Int. Res. J. Pharm. 2014; 5(9):http://dx.doi.org/
10.7897/2230-8407.0509140

Source of support: Nil, Conflict of interest: None Declared