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Original Article

The Relationship between Aortic Clamping Time and Platelet-lymphocyte Ratio in Isolated Coronary Artery Bypass Surgery

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Abstract

Objectives: This study aims to evaluate the relationship between aortic clamp duration acute coronary syndrome (ACS) and platelet-to-lymphocyte ratio (PLR) in patients undergoing isolated coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB).

Methods: This retrospective study included 96 patients who underwent elective isolated CABG at a single center between June 2021 and September 2023. Patients were divided into two groups according to median ACS: Group I (ACS <66.2 min, n=54) and Group II (ACS >66.2 min, n=42). Demographic data, pre-operative and 24-h post-operative platelet and lymphocyte counts, and operative details were recorded. PLR was calculated using the platelet/lymphocyte formula. Statistical analyses were performed using IBM Statistical Packages for the Social Sciences 25.0.

Results: The mean ages of Group I and Group II were 63.6±8.8 and 66±8.9 years, respectively (p>0.05). There was no significant difference in pre- and post-operative PLR values between the groups (p>0.05). There was no correlation between post-operative PLR and the duration of CPB and ACS (p>0.05). However, there was a strong positive correlation between CPB and ACS durations (p<0.001).

Conclusion: The study revealed that there was no significant correlation between post-operative PLR and perioperative ACS and CPB durations. While post-operative PLR increased significantly in both groups, this increase was not associated with the duration of ACS or CPB. PLR may be a useful biomarker in determining inflammation and adverse outcomes in CABG, but larger-scale, randomized, prospective studies are needed to confirm these findings.

Keywords: Aortic clamping time; cardiopulmonary bypass; coronary artery bypass graft; platelet-to-lymphocyte ratio.

İzole Koroner Arter Bypass Cerrahisinde Aort Klemp Süresi ile Trombosit-lenfosit Oranı Arasındaki İlişki

Özet

Amaç: Bu çalışmada kardiyopulmoner baypas (KPB) ile izole koroner arter baypas greftleme (KABG) yapılan hastalarda aortik klemp süresi (AKS) ile trombosit/lenfosit oranı (PLR) arasındaki ilişkinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Bu retrospektif çalışmaya Haziran 2021 ile Eylül 2023 tarihleri arasında tek bir merkezde elektif izole KABG uygulanan 96 hasta dahil edildi. Hastalar medyan AKS'ye göre iki gruba ayrıldı: Grup I (AKS < 66.2 dakika, n=54) ve Grup II (AKS > 66.2 dakika, n=42). Demografik veriler, ameliyat öncesi ve 24 saat sonrası trombosit ve lenfosit sayıları ve ameliyat ayrıntıları kaydedildi. PLR trombosit/lenfosit formülü kullanılarak hesaplandı. İstatistiksel analizler IBM SPSS 25.0 kullanılarak yapıldı.

Bulgular: Grup I ve Grup II'nin ortalama yaşları sırasıyla 63.6±8.8 ve 66±8.9 idi (p>0.05). Ameliyat öncesi ve sonrası PLR değerleri açısından gruplar arasında anlamlı fark yoktu (p>0.05). Ameliyat sonrası PLR ile KPB ve AKS süresi arasında korelasyon yoktu (p>0.05). Ancak, KPB ve AKS süreleri arasında güçlü bir pozitif korelasyon vardı (p<0.001).

Sonuç: Çalışmada postoperatif PLR ile perioperatif AKS ve KPB süreleri arasında anlamlı bir korelasyon olmadığı görüldü. Ameliyat sonrası PLR her iki grupta da anlamlı olarak artarken, bu artış AKS veya KPB süresi ile ilişkili değildi. PLR, KABG'de enflamasyon ve olumsuz sonuçları belirlemede faydalı bir biyobelirteç olabilir, ancak bu bulguları doğrulamak için daha büyük ölçekli, randomize, prospektif çalışmalara ihtiyaç vardır.

Anahtar sözcükler: Aortik klemp süresi; kardiyopulmoner baypas; koroner arter baypas grefti; trombosit/lenfosit oranı.

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Introduction

Coronary artery bypass grafting (CABG) is an important surgery in which blockages in a patient's coronary arteries are bypassed by venous or arterial routes. This procedure restores blood flow to the ischemic myocardium, restoring vitality and relieving anginal symptoms. In general, this procedure is completed using cardiopulmonary bypass (CPB).[1]

Despite advances in extracorporeal circulation, CPB may cause post-operative morbidity by inducing an inflammatory reaction throughout the body.[2] This inflammatory response mainly involves the activation of complement proteins induced by the activating effect of a foreign surface and heparin-protamine complex.[3] Vasoconstriction, increased capillary permeability, activation of leukocytes, and aggregation of platelets are facilitated by complement proteins.[4]

Decreased platelet counts are frequently encountered after CABG. Post-operative low platelet count has been shown to be associated with poor prognosis.[5] However, many parameters have been investigated to follow the inflammatory process in the post-CABG period. Platelet-to-lymphocyte ratio (PLR) is an inflammatory biomarker used prognostically in various diseases.[6]

The marked increase in inflammation after CABG may be related to perioperative CPB and aortic clamping times acute coronary syndrome (ACS). The association of PLR with perioperative times in CPB-treated CABG procedures is unclear. The aim of this study was to evaluate the relationship between aortic clamp time and toll-like receptors in isolated coronary artery bypass surgery.

Materials and Methods

Study Population

This retrospective study consisted of 96 patients who underwent elective isolated CABG procedures at a single center between June 2021 and September 2023. Patients over 18 years of age who underwent isolated coronary artery bypass surgery with CPB were included. Patients with reoperation, patients with additional cardiac surgical procedures, patients with known cerebrovascular and bleeding pathology, and patients with missing medical data were excluded. The study was approved by Bandirma Onyedi Eylül University Non-Interventional Research Ethics Committee with the ethics committee decision dated June 13, 2024 and numbered 2024-135. The flow chart of the current study is shown in Figure 1.

The study groups were formed by calculating the median aortic clamp times of the total population (n=96). Accordingly, patients with aortic clamping times below 66.2 min were defined as Group I (n=54) and patients with aortic clamping times above 66.2 min were defined as Group II (n=42).

Demographic data, pre- and post-operative 24 h platelet and lymphocyte counts and operative data were recorded. PLR was calculated as the ratio of platelets (10^3/uL) to lymphocytes (10^3/uL) obtained from pre-operative and 24-h post-operative blood samples.

Operative Technique

In our clinic, all patients were operated under general anesthesia through a median sternotomy and systemic heparin administration (300 IU/kg) followed by cannulation of the ascending aorta and right atrium under CPB. Standard CPB circuit and surgical management were used. All patients received antegrade and retrograde combined isothermic and hyperkalemic blood cardioplegia. Surgery was performed under moderate systemic hypothermia (28–32°C). During CPB, CPB flow was maintained at 2.2–2.5 L/min/m^2, mean perfusion pressure at 60–80 mmHg, and hematocrit level between 20 and 25%. Distal anastomoses were performed during aortic cross-clamping and proximal anastomoses were performed on the ascending aorta using lateral clamping over the beating heart. After the surgical procedure was completed, the patient's body temperature was raised to 37°C and CPB was terminated. Decannulation was performed after neutralization with protamine.

Statistical Analysis

Statistical analysis was performed using the IBM (Statistical Packages for the Social Sciences [SPSS]) 25.0 (SPSS Inc., Chicago, IL, USA) package program. The conformity of the data to normal distribution was evaluated by the Shapiro–Wilks test, histogram, and box plot graphs. Student-t test and Mann–Whitney U-tests were used to compare the two groups that conformed to a normal distribution and those that did not, respectively. The paired samples test was used to analyze the pre- and post-operative measurements within the groups if

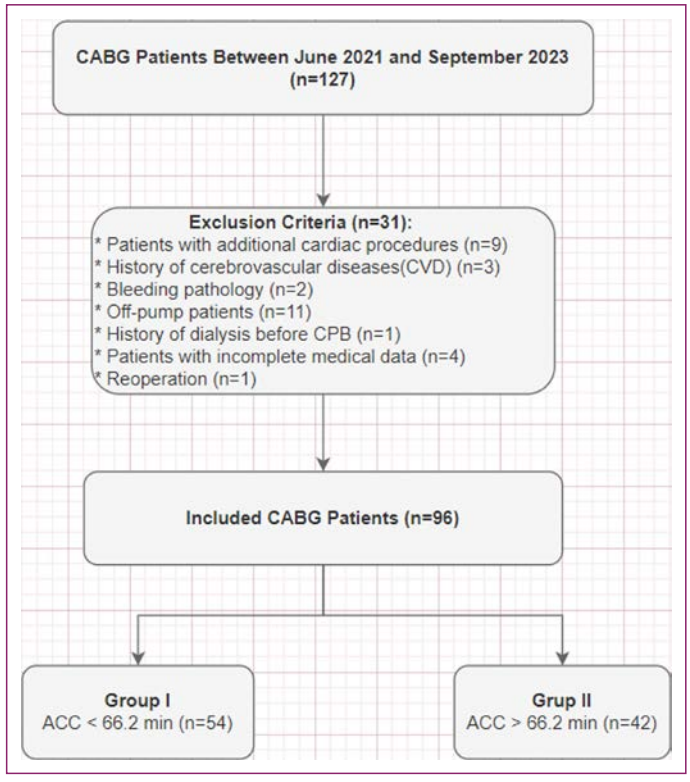

Figure 1. Flow chart the study.

CABG: Coronary artery bypass grafting; ACC: Aortic cross clamp.

Table 1. Demographic and operative data of the patients

Variables	Group I (n=54) Mean±SD	Group 2 (n=42) Mean±SD	p
Gender (male), n (%)	35 (64.8)	31 (73.8)	
Age	63.6±8.8	66±8.9	0.189
BMI	28.3±4.1	27.9±3.5	0.677
BSA (m^2)	1.84±0.17	1.88±0.14	0.156
Ejection fraction (%)	48.8±5.6	48.0±6.3	0.499
CPB (min)	103.8±20	134.4±21.3	<0.001**
ACC (min)	51.7±10.7	89.9±13.0	<0.001**

**: p<0.001. SD: Standard deviation; BMI: Body mass index; BSA: Body surface area; CPB: Cardiopulmonary bypass; ACC: Aortic cross clamp.

there was conformity to normal distribution, and the Wilcoxon test was used if there was non-conformity to normal distribution. Pearson or Spearman correlation test was used to evaluate the relationship between variables depending on the distribution. The results were evaluated at a 95% confidence interval and significance was evaluated at p<0.05 level.

Results

A total of 96 patients who underwent isolated CABG were included in the study. The mean ages of the patients included in the study were 63.6±8.8 years for group I and 66±8.9 years for group II (p>0.05). 64.8% of patients in group I and 73.8% of patients in group II were male. The mean duration of CPB was 103.8±20 min for group I and 134.4±21.3 min for group II (p<0.05). The mean aortic clamping times were 51.7±10.7 min for group I and 89.9±13.0 min for group II (p<0.05) (Table 1).

The PLR changes within and between the groups at pre- and post-operative 24th-h periods are shown in Table 2. In group I and group II, there was a significant difference between pre- and post-operative PLR values at 24 h. However, no statistical difference was found between pre- and post-operative PLR levels in the comparison between the groups (p>0.05) (Table 2). The graphical changes of PLR, platelet, and lymphocyte levels in group I and group II are shown in Figures. 2 and 3.

There was no correlation between post-operative PLR and CPB and aortic clamp times (p>0.005). However, there was a strong positive correlation between the duration of CPB and aortic clamping times (p<0.001).

Discussion

The pathophysiology associated with PLR during atherosclerotic processes in coronary artery disease and ACS is complex. In general, the value of the PLR index correlates with the immune response, indicating the degree of inflammatory response. An increased PLR index may indicate ongoing pro-inflammatory processes.[7] In this study, we investigated the variation of platelet, lymphocyte, and PLR parameters according to aortic clamping time in patients undergoing isolated CABG surgery.

In the human body, platelets play important roles in hemostasis, tissue regeneration, and synthesis of adhesion molecules.[8] Platelet activation occurring in cardiac surgery with CPB may lead to post-operative myocardial infarction and stroke.[9] This condition has also been associated with prolonged intensive care unit stay, increased mortality, and renal failure.[10]

Thrombocytopenia is common following cardiac surgery with CPB. In some studies, it has been reported that the mean platelet decrease ranges between 30 and 50%.[11] In addition, an absolute decrease in lymphocyte counts after CPB has been reported.[12] Similar to the studies conducted in our study, post-operative platelet and lymphocyte counts decreased in both groups. Although there was a significant difference in these values for both periods within the groups, post-operative platelet, and lymphocyte counts were found to be similar between the groups. This indicates that platelets and lymphocytes change at a similar rate during intermediate aortic clamping periods.

Table 2. Comparison of pre- and post-operative parameters

	Group		p
	Group I (n=54)	Group 2 (n=42)	
Platelet counts (10^3/μL)			
Pre-operative, mean±SD	274.4±76.7	247.8±84.4	0.110[b]
Post-operative, mean±SD	198.2±65.6	168.5±53.3	0.019[b]
p[c]	0.001**	0.001**	
Change Δ, mean±SD	76.3±62.3	79.3±68.5	0.001**
Lymphocyte Counts (10^3/μL)			
Pre-operative, mean±SD	2.11±0.6	2.07±0.7	0.665[b]
Post-operative, mean±SD	1.0±0.4	0.9±0.4	0.502[b]
p[c]	0.001**	0.001**	
Change Δ, mean±SD	1.12±0.7	1.16±0.7	0.001**
PLR			
Pre-operative, mean±SD	142.6±62.9	129.9±52.7	0.379[b]
Post-operative, mean±SD	228.6±101.4	207.4±97.3	0.268[b]
p[c]	0.001**	0.001**	
Change Δ, mean±SD	-86.0±110.8	-77.4±90.7	0.001**

**: p<0.001. [b]: Mann–Whitney U-Test; [c]: Wilcoxon test. SD: Standard deviation; PLR: Platelet lymphocyte ratio.

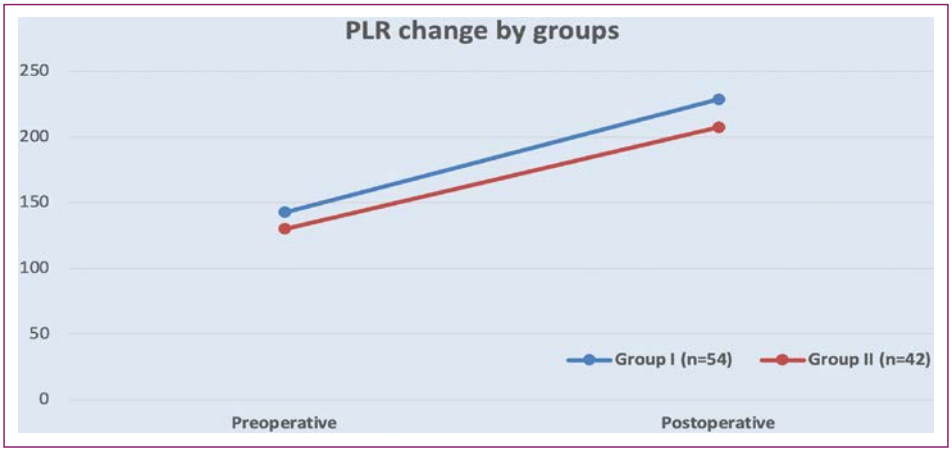

Figure 2. Platelet-to-lymphocyte ratio changes according to groups.

PLR: Platelet lymphocyte ratio.

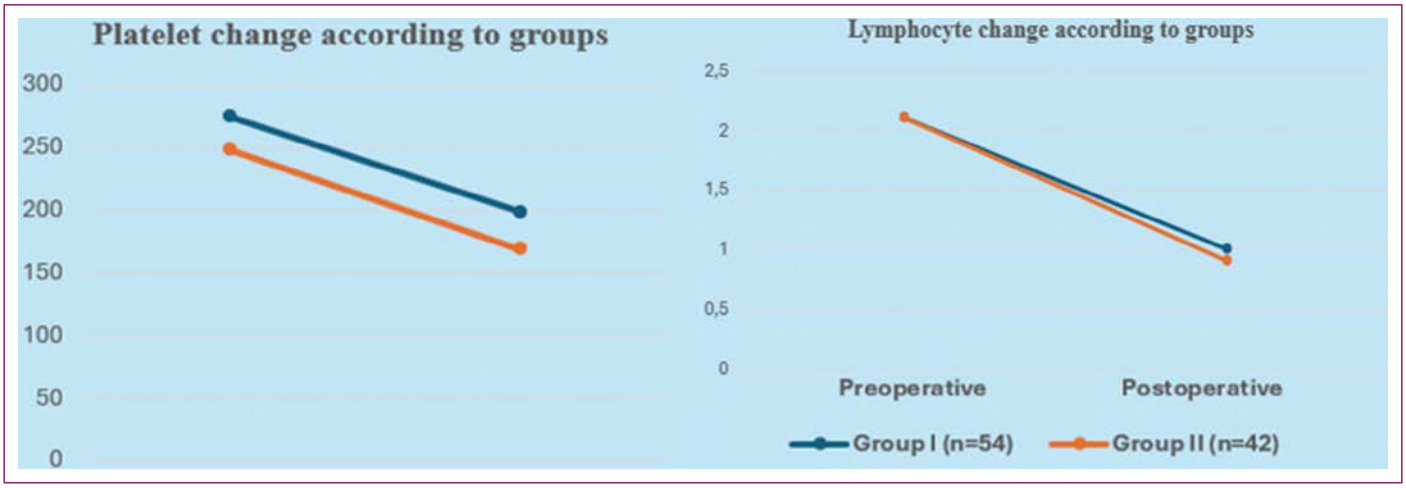

Figure 3. Changes of platelet and lymphocytes in the groups.

The variation of PLR in coronary artery bypass surgery has not been clearly investigated. Some previous studies aimed to determine the difference between PLR and clinical prognosis in patients with ACS. Li et al.[13] reported that individuals with higher PLR had a higher risk of adverse in-hospital outcomes. The pathophysiology associated with PLR during coronary artery disease and CPB processes remains unclear. The decrease in absolute platelet and lymphocyte counts during CPB increases the post-operative PLR level. In our study, a statistically significant increase in pre- and post-operative PLR was detected in both groups.

In general, it is emphasized that the value of the PLR index is related to the immune response and indicates the degree of inflammatory response.[7] CPB and aortic cross-clamping procedures in open heart surgery have mechanisms that trigger systemic inflammation.[14] In our study, the PLR value showed a significant increase in the post-operative period compared to the pre-operative period, indicating that it can be used as a marker of inflammation. However, this increase was not correlated with the CPB and aortic cross-clamp times associated with coronary artery bypass surgery. In addition to C-reactive protein and white blood cell parameters, which are non-specific markers of inflammation in coronary artery bypass surgery, we emphasize that PLR value can be used as a useful biomarker in inflammation and detection of major adverse events.

Table 3. Correlation of variables with each other

Variables	Post-operative PLR	Post-operative platelet	Post-operative lymphocyte
CPB			
r	-0.014	-0.043	-0.038
p	0.893	0.680	0.714
ACC			
r	-0.050	-0.216	-0.144
p	0.631	0.034*	0.161
Post-operative PLR			
r	–	0.407	-0.632
p		0.001**	0.001**

*: p<0.05; **: p<0.001. CPB: Cardiopulmonary bypass; ACC: Aortic cross clamp; PLR: Platelet-lymphocyte ratio; r: Spearman Correlation test.

Our study had some limitations. One of them was that it was single-centered and had a small sample size. This causes the power of the study to be low. Another limitation was the observational and non-randomized design of the study.

Conclusion

Our study found that the PLR significantly increased in the post-operative period compared to the pre-operative period in patients undergoing isolated CABG. This increase suggests that PLR can serve as a marker of inflammation. However, there was no correlation between the CPB and aortic clamp times with the post-operative PLR levels. While the PLR value can be a useful biomarker for inflammation and detection of major adverse events in CABG, it is not influenced by the duration of CPB or aortic clamping. Future research with larger sample sizes and randomized designs is necessary to further explore the role of PLR in the context of open-heart surgery.

Disclosures

Ethics Committee Approval: The study was approved by the Bandirma Onyedi Eylül University Non-Interventional Research Ethics Committee (no: 2024-135, date: 13/06/2024).

Authorship Contributions: Concept – D.D.; Design – S.G.; Supervision – S.G.; Funding – D.D.; Materials – S.G.; Data collection and/or processing – D.D.; Data analysis and/or interpretation – S.G.; Literature search – D.D.; Writing – S.G.; Critical review – D.D.

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References

1. Alexander JH, Smith PK. Coronary-artery bypass grafting. N Engl J Med 2016;375(10):e22. DOI: 10.1056/NEJMc1608042.
2. Wan S, LeClerc JL, Vincent JL. Inflammatory response to cardiopulmonary bypass: Mechanisms involved and possible therapeutic strategies. Chest 1997;112(3):676–92. DOI: 10.1378/chest.112.3.676.
3. Wan S, Yim AP. Cytokines in myocardial injury: İmpact on cardiac surgical approach. Eur J Cardiothorac Surg 1999;16 Suppl 1:S107–11. DOI: 10.1016/s1010-7940(99)00200-6.
4. Schwartz JD, Shamamian P, Schwartz DS, Grossi EA, Jacobs CE, Steiner F, et al. Cardiopulmonary bypass primes polymorphonuclear leukocytes. J Surg Res 1998;75:177–82. DOI: 10.1006/jsre.1997.5287.
5. Kertai MD, Zhou S, Karhausen JA, Cooter M, Jooste E, Li YJ, et al. Platelet counts, acute kidney ınjury, and mortality after coronary artery bypass grafting surgery. Anesthesiology 2016;124(2):339–52. DOI: 10.1097/ALN.0000000000000959.
6. Yildiz A, Yuksel M, Oylumlu M, Polat N, Akyuz A, Acet H, et al. The utility of the platelet-lymphocyte ratio for predicting no reflow in patients with ST-segment elevation myocardial ınfarction. Clin Appl Thromb Hemost 2015;21(3):223–8. DOI: 10.1177/1076029613519851.
7. Tamaki S, Nagai Y, Shutta R, Masuda D, Yamashita S, Seo M, et al Combination of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios as a novel predictor of cardiac death in patients with acute decompensated heart failure with preserved left ventricular ejection fraction: A multicenter study. J Am Heart Assoc 2023;12(1):e026326. DOI: 10.1161/JAHA.122.026326.
8. Karagoz I, Aktas G, Yoldas H, Yildiz I, Ogun MN, Bilgi M, et al. Association between hemogram parameters and survival of critically ıll patients. J Intensive Care Med 2019;34(6):511–3. DOI: 10.1177/0885066617703348.
9. Ranucci M. Hemostatic and thrombotic issues in cardiac surgery. Semin Thromb Hemost 2015;41(1):84–90. DOI: 10.1055/s-0034-1398383.
10. Williamson DR, Albert M, Heels-Ansdell D, Arnold DM, Lauzier F, Zarychanski R, et al. Thrombocytopenia in critically ill patients receiving thromboprophylaxis: Frequency, risk factors, and outcomes. Chest 2013;144(4):1207–15. DOI: 10.1378/chest.13-0121.
11. Agarwal S, Johnson RI, Kirmani BH. Pre- and post-bypass platelet function testing with multiple electrode aggregometry and TEG platelet mapping in cardiac surgery. J Cardiothorac Vasc Anesth 2015;29(5):1272–6. DOI: 10.1053/j.jvca.2015.01.028.
12. Rinder CS, Mathew JP, Rinder HM, Tracey JB, Davis E, Smith BR. Lymphocyte and monocyte subset changes during cardiopulmonary bypass: Effects of aging and gender. J Lab Clin Med 1997;129(6):592–602. DOI: 10.1016/s0022-2143(97)90193-1.
13. Li W, Liu Q, Tang Y. Platelet to lymphocyte ratio in the prediction of adverse outcomes after acute coronary syndrome: A meta-analysis. Sci Rep 2017;7:40426. DOI: 10.1038/srep40426.
14. Dabbagh A, Rajaei S, Bahadori Monfared A, Keramatinia AA, Omidi K. Cardiopulmonary bypass, ınflammation and how to defy it: Focus on pharmacological interventions. Iran J Pharm Res 2012;11(3):705–14.