



Scholars Research Library

Der Pharmacia Lettre, 2012, 4 (4):1188-1193  
(<http://scholarsresearchlibrary.com/archive.html>)



## Piroxicam flash tablet relieves post-operative pain faster than piroxicam regular tablet (A Randomised, Controlled Trial)

Shrikant Deshpande and Nagesh Naik

Dept. of Orthopaedics, Bharati Vidyapeeth Deemed University Medical College, & Hospital, Sangli

### ABSTRACT

To compare the onset of analgesic action of Piroxicam flash tablet (FT) with that of piroxicam regular (RT) in post-operative pain. Randomized, controlled, parallel-group trial. Indoor patients of the department of Orthopaedics, Government Medical College, Miraj. 39 men and women over 18 years of age undergoing orthopaedic operations and giving written informed consent for the study. Piroxicam Ft (10 mg) sublingually or piroxicam regular (10 mg) tablet orally, by randomized assignment. One tablet when patient demanded pain relief after operation and then one tablet in the morning and one in the evening for 7 days. Primary: onset of pain relief, defined as time in minutes required for initial pain intensity to fall by  $\geq 50\%$  as measure on a visual analogue scale (VAS), then before the morning and the evening doses for the 7 days, along with tenderness and inflammation scores. Secondary: Proportion of patients requiring addition analgesic for pain relief. 20 patients (13 M, 7 F; mean age 47.6 year [SD 15.32]) received FT, and 19 patients (12 M, 7 F; mean age 55.6 year [SD 21.32]) received RT. The time for onset of action was 10.42 minutes (SD 9.41) for FT and 18.83 minutes (SD 13.41) for RT. The difference of 8.4 minutes was significant by *t*-test ( $p = 0.036$ ; 95% CI: -16.23 to -0.59). Both formulations showed a statistically significant reduction ( $p < 0.001$ ) in pain, tenderness and inflammation as compared with baseline values. 3 of 20 patients (15 %) given FT and 6 of 19 patients (32%) given RT required additional analgesics ( $p = 0.63$  by  $\chi^2$  test). Piroxicam FT has a faster onset of analgesic action as compared with piroxicam RT in pain following orthopaedic operations. The analgesic and anti-inflammatory activity of both the formulations are comparable.

**Key words:** sublingual piroxicam, postoperative pain and onset of analgesia.

### INTRODUCTION

Piroxicam is a non-steroidal anti-inflammatory drug (NSAID) commonly used to relieve post-operative pain. Like other NSAIDs, its main mechanism of action is by inhibition of the cyclooxygenase enzyme, resulting in reduced prostaglandin synthesis, which is responsible for pain and inflammation. Piroxicam also inhibits thromboxane synthesis in platelets and thus inhibits the secondary phase of platelet aggregation. Since platelets can be involved in the inflammatory process, this action may contribute to the efficacy of piroxicam(2)

Piroxicam has a long half-life, but due to its slower absorption in the gastrointestinal tract its onset of action is also slow. When administered orally, it takes more than 30 minutes to produce appreciable relief of pain. Any formulation that could expedite the absorption of the active ingredient, and thereby the onset of analgesia, could therefore have a practical benefit in the management of post-operative pain. With this in view, a formulation of piroxicam, termed flash tablet (FT), was developed by Emcure Pharmaceuticals which, when administered

sublingually, was observed to dissolve almost instantaneously and produce therapeutic serum levels of piroxicam earlier than the conventional piroxicam tablet(1) As such a formulation would be expected to induce analgesia earlier than a conventional formulation; we carried out a comparative trial of piroxicam FT and conventional Piroxicam tablet to assess the onset of analgesia with them.

### **Patients and Methods**

The trial was carried out at the Department Orthopaedics, Govt. Medical College, Miraj between December, 2001 and March 2002.

**Study Design:** the trial was randomized, controlled, parallel group.

**Patients:** 39 patients (25 men, 14 women) with mean age 50.87 (+18.88) years who had undergone orthopaedic surgery were enrolled in the study. All patients gave written informed consent. Patients hypersensitive to NSAIDs, having gastric or duodenal ulceration, or receiving any other of additional analgesics were excluded from the trial.

**Medications:** the patients were randomly assigned to two groups of 20 each, one receiving piroxicam FT (each containing 10 mg) sublingually, and the other receiving piroxicam regular tablet (each containing 10 mg ) orally. Both the test and control drugs were exactly similar in shape, size and appearance. The first tablet of the assigned medication was given when the patient complained of pain after the operation and sought medication for titts relief. Subsequently, the medication was given twice a day, morning and evening, for 7 days.

### **Randomization:**

Randomization was done in blocks of 10 with the help of computer based program (True epistat Standard version 1999). The patients were enrolled in a chronological order as per the randomization chart.

**Assessment of response:** an observer who was kept unaware of the medication received by the patient, helped the patients to assess their pain on a 10-cm. Visual analogue scale, before giving the first dose: then every 5 minutes until the initial score fell by 50% ; and then before giving each subsequent dose every morning and evening for 7 days. The time required for the initial score to fall by 50% was taken as the time of onset for analgesia. Tenderness and inflammation were also assessed by the observer on a 10-cm. visual analogue scale: before giving the first dose, and then before giving each subsequent dose up to 7 days.

Besides, the patients and the investigator independently recorded their opinion about the usefulness of the treatment at the end of the trial, i.e. on day 7, as ineffective, moderately effective and effective.

Any observed or reported adverse events were recorded with their nature, intensity, actions taken and outcome.

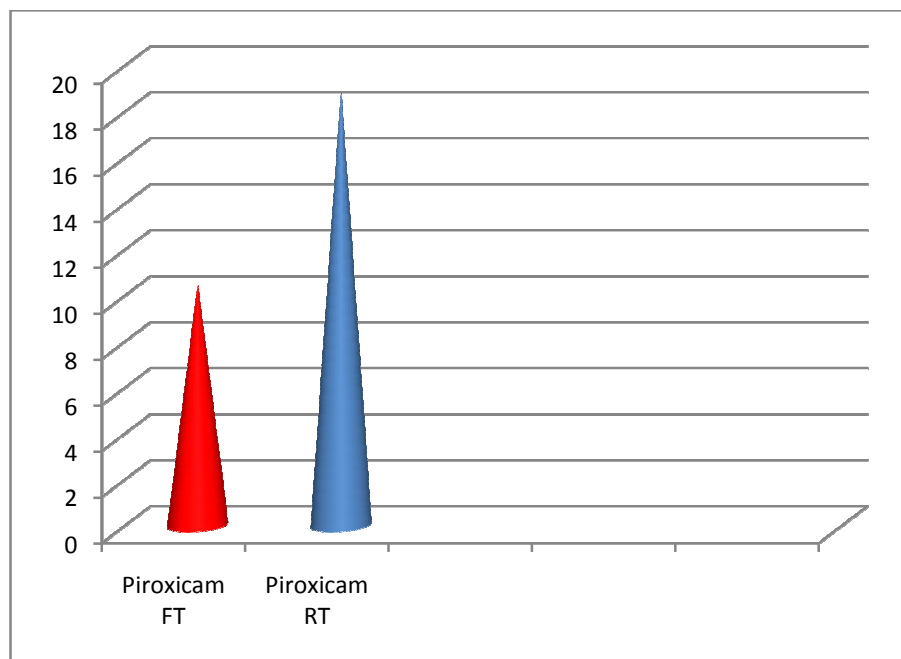
**Statistical analysis:** The evaluable patients were analyzed for baseline comparability of the groups for sex distribution, age, anesthesia, and initial scores of pain, tenderness and inflammation.

The mean time for onset of analgesia was computed for each group, and the difference between them tested for significance by t-test for unpaired data. The difference between the means of symptoms such as pain, inflammation and tenderness were analyzed using Student's t-test. The patients' opinion and the investigator's opinion about the treatment were compared using the Kappa reliability test.

## **RESULTS**

The onset of opinion of piroxicam Flash tablet was recorded as  $10.42 \pm 9.41$  (men  $\pm$  SD) minutes after administration of the first tablet whereas for piroxicam regular tablet it was  $18.83 \pm 13.41$  minutes. (Fig-1) The difference of 8.4 minutes was significant by t-test ( $p = 0.036$ ; 95% CI: -16.23 to -0.59)

Figure 1. Onset of action of Piroxicam FT and Piroxicam RT

**Confidential Report**

The mean scores  $\pm$  SE for pain, inflammation and tenderness are given in table -1. There was no statistically significant difference between the baseline values of the two groups ( $p > 0.05$ ). The score in the piroxicam FT group were ( $3.38 \pm 1.86$  for pain,  $3.63 \pm 1.78$  for inflammation &  $3.55 \pm 1.55$  for tenderness ) while the score for piroxicam RT were higher (  $3.7 \pm 1.37$  for pain,  $3.95 \pm 1.89$  for inflammation &  $3.93 \pm 1.87$  for tenderness).

The total mean score for pain reduced from  $3.09 \pm 1.82$  on day 1 to  $1.25 \pm 1.65$  on day 7 with piroxicam FT (59.55 % reduction) ( $p < 0.05$ ) and from  $3.42 \pm 1.82$  ( $< 0.05$ ) on day 1 to  $1.47 \pm 1.65$  on day 7 (57.31 % reduction with piroxicam RT (Fig.-2).

Table 1. Mean scores for pain, inflammation and tenderness for both treatment Groups

	Pain		Tenderness		Inflammation	
	Piroxicam FT	Piroxicam conventional	Piroxicam FT	Piroxicam conventional	Piroxicam FT	Piroxicam conventional
Day 1	$3.09 \pm 1.82$	$3.42 \pm 1.82$	$3.31 \pm 1.45$	$3.67 \pm 1.45$	$3.46 \pm 1.69$	$3.78 \pm 1.69$
Day 2	$2.56 \pm 1.41$	$3.03 \pm 1.41$	$2.93 \pm 1.53$	$3.17 \pm 1.53$	$2.53 \pm 1.71$	$3.125 \pm 1.71$
Day 3	$2.03 \pm 1.60$	$2.53 \pm 1.60$	$2.40 \pm 1.71$	$2.67 \pm 1.66$	$2.03 \pm 1.66$	$2.67 \pm 1.66$
Day 4	$1.62 \pm 1.75$	$2 \pm 1.75$	$2.15 \pm 1.96$	$2.28 \pm 1.87$	$1.81 \pm 1.87$	$2.28 \pm 1.87$
Day 5	$1.37 \pm 1.79$	$1.89 \pm 1.79$	$1.90 \pm 1.98$	$1.96 \pm 1.90$	$1.56 \pm 1.90$	$1.96 \pm 1.90$
Day 6	$1.31 \pm 1.76$	$1.67 \pm 1.76$	$1.75 \pm 2.04$	$1.75 \pm 2.12$	$1.375 \pm 2.12$	$1.75 \pm 2.12$
Day 7	$1.25 \pm 1.65$	$1.46 \pm 1.65$	$1.62 \pm 1.92$	$1.71 \pm 2.12$	$1.375 \pm 2.12$	$1.71 \pm 2.12$

At the end of day 7 the mean scores for inflammation in piroxicam FT group reduced from  $3.46 \pm 1.69$  on day 1 to  $1.375 \pm 2.12$  on day 7 (60.27% reduction ) as compared to  $3.785 \pm 1.69$  on day 1 in piroxicam RT which reduced to  $1.71 \pm 2.12$  (54.77% reduction) (Fig. – 3).

There was complete resolution of inflammation in the piroxicam FT group in 20% of patients, whereas the resolution in the piroxicam RT was found to be only in 5% cases.

Figure 2. Reduction in pain for Piroxicam FT and Piroxicam RT Percentage reduction in mean pain

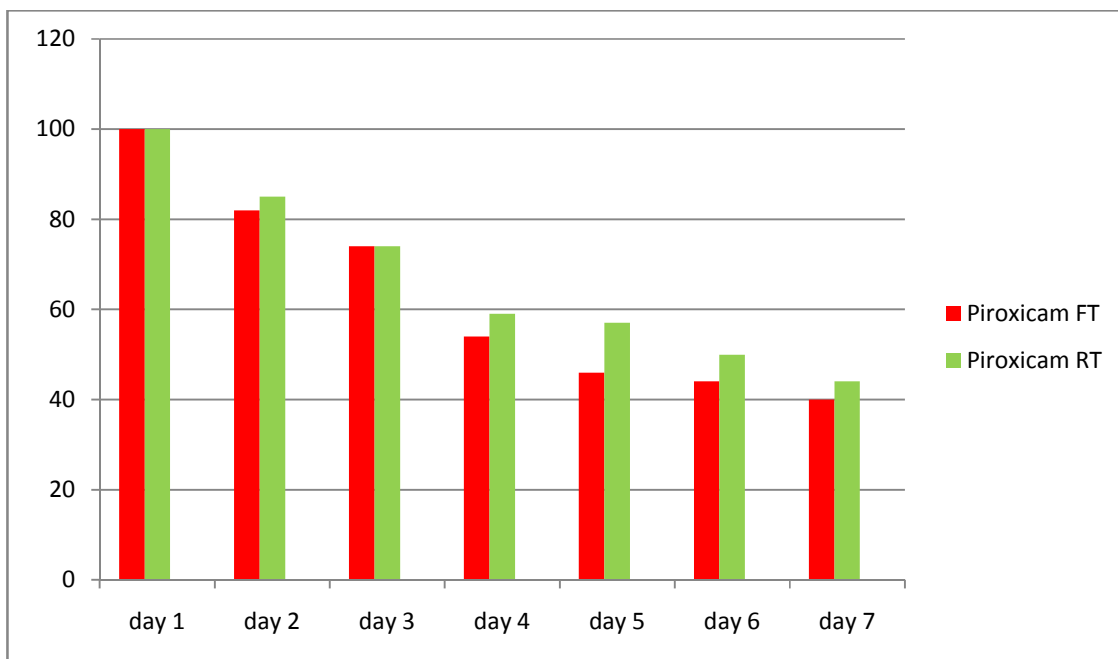
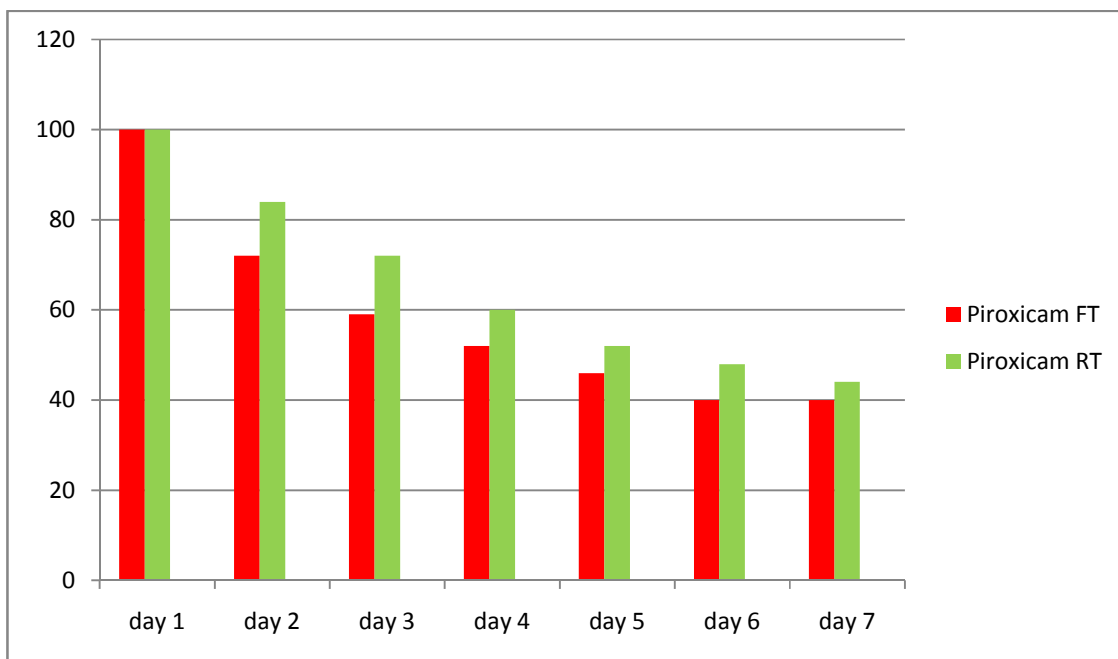
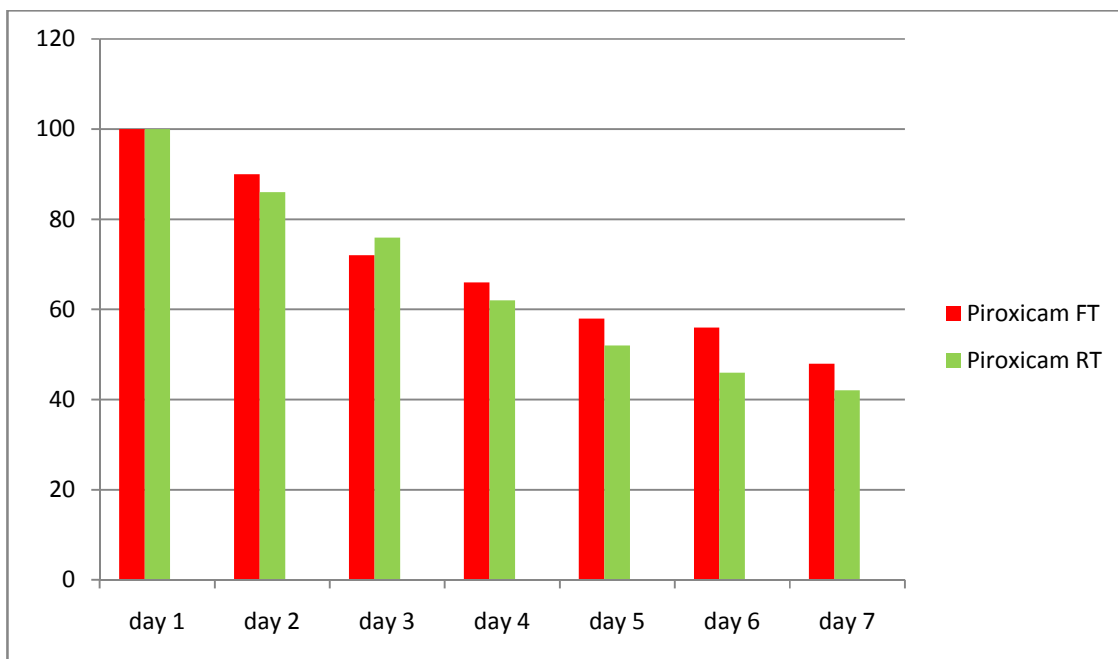


Figure 3. Reduction in inflammation for Piroxicam FT and Piroxicam RT Percentage reduction in inflammation



At the end of day 7, the sores for tenderness reduced from  $3.31 \pm 1.45$  to  $1.625 \pm 1.92$  (51.06 % reduction ) in the piroxicam FT group while, in the piroxicam RT group it reduced from  $3.67 \pm 1.45$  to  $1.57 \pm 1.92$  (57.23 % reduction ) (Fig.- 4).

**Figure 4. Reduction in tenderness for Piroxicam FT and Piroxicam RT Percentage reduction in tenderness**

The investigator's and the patient's opinion on the efficacy of the treatment were compared, using Kappa test and they were found to be similar ( $\kappa = 0.76$ ) suggesting uniformity of opinion ( $p < 0.001$ ). 31.25 % patients reported the therapy to be highly effective in the piroxicam FT group as compared to 28.57% in the piroxicam RT group. In the opinion of the investigation the therapy was highly effective in 25 % of the patients in the piroxicam FT group as compared to 21.43 % in the piroxicam RT. None of the patients on piroxicam FT complained of any adverse effects whereas 1 patient in the piroxicam RT complained of gastric irritation & acidity. Six patients (32%) in the piroxicam RT group and 3 (15%) in the piroxicam FT group required additional analgesics in the form of diclofenac injections during the study.

### DISCUSSION

NSAIDs have been used for more than 25 years to treat rheumatological disease. They were then introduced to relieve pain after tooth extraction and to provide post-operative analgesia. When used alone, they are effective in relieving minor to moderate pain such as that seen after maxillofacial, minor orthopaedic or some ambulatory surgical procedures and postpartum pain (2)

NSAIDs have additional anti-inflammatory activity, lacking in opioids, which plays an important role in relieving post-operative pain and inflammation.

In the present study, it was observed that the onset of action of sublingually administered piroxicam FT (10mg) is only 10.42 minutes as compared to 18.83 minutes with piroxicam regular tablets. Such a formulation provides faster reduction of symptoms as compared to conventional oral formulation in acute trauma cases, thereby offsetting the use of parenteral analgesics. In a separate study done on piroxicam fast dissolving dosage form (FDDF) for sublingual administration, in the treatment of primary dysmenorrhea it was observed that piroxicam (40 mg) showed its analgesic efficacy 15 minutes after the drug administration (3). This early onset (15 minutes) of piroxicam FDDF (40 mg) was also observed in a study on patients with migraine (4). Fast oral dissolution technology is suitable for pts who are not having access to water such as travelling pts, bedridden patients (5).

. In a study comparing piroxicam FDDF (40 mg) with intramuscular diclofenac, piroxicam FDDF was found to be as effective as parenteral diclofenac in emergency renal colic treatment. Furthermore, its ease of self-administration was found to increase patient compliance and potential use in general practice (6)

Piroxicam has been reported to be well tolerated in children(7) and this, together with early onset of action of this flash tablet is an attractive alternative to parenteral analgesics in pediatrics. In two separate trials done on piroxicam fast dissolving dosage form (FDDF), it was observed that piroxicam FDDF showed a significant relief of pain compared to naproxen sodium (8) and aspirin (9)

In a separate study on patients with endodontic pain, piroxicam provided more consistent and rapid relief of pain than diclofenac when assessed for 3 consecutive days after dental surgery (10) This study demonstrates faster analgesic activity of piroxicam FT, which would relieve the patient's distress much earlier than diclofenac.

Both the formulations showed a significant reduction in pain, tenderness and inflammation scores. Piroxicam FT showed a greater relief in total symptoms as compared to Piroxicam RT consistently from Day 1 to Day 7 (Fig 2). There was complete resolution of inflammation in the piroxicam FT group in 20% of cases whereas it was seen in only 5% cases with Piroxicam conventional group.

In a study comparing piroxicam and diclofenac in 40 rheumatoid arthritis patients, piroxicam exercised a significant action on the inflammation-specific parameters (reduction of the alpha 2-globulin fraction by 0.75 %), whereas diclofenac did not (11) This indicates a better anti-inflammatory activity of piroxicam FT, which would aid wound healing, thereby facilitating early discharge of hospitalized patients.

In non-rheumatic conditions also, piroxicam was shown to be superior to most of the other NSAIDs (12) It also offers a prolonged duration of action due to a longer plasma half-life (13)

None of the patients on piroxicam FT reported any adverse effects whereas one patient on Piroxicam RT complained of gastric irritation & severe acidity. The adverse effects of piroxicam were reported to be similar to other NSAIDs (14) Tolerability of Piroxicam FDDF was rated high in a study evaluating its efficacy in acute low back ache (15)

## CONCLUSION

Piroxicam flash tablet relieves postoperative pain earlier than Piroxicam regular tablet. The analgesic and anti-inflammatory activity of both the formulations are comparable. Both formulations were found to be safe.

## REFERENCES

- [1] Data on Files – Emcure Pharmaceuticals.
- [2] Forrest J. Acute Pain: Pathophysiology and Treatment **1998**, London: Manticore Publishers : 174.
- [3] Ragni N and Ciccarelli A. *Minerva Ginecol* **1993** ; 45 (7-8) ; 365-75.
- [4] Nappi G, Micieli G, Tassorelli C, Viotti E Altavilla T. *Headache* **1993** June ; 33 (6) : 296-300.
- [5] Debjit bhowmik, Chiranjib, Jyoti jaiswal: *Der pharmacia Lettre*, scholars research library **2009**, 1(2), 262 -276
- [6] Supervia A, Pedro –Botet J, Nogues X, Echarte JL, Minguez S, Iglesias ML, Gelabert A *Br J Urol* **1998** Jan ; 81 (1) : 27-30.
- [7] Garcio MO, Maldonado CJA, Cuttica R, Garay SM. *Eur J Rheumatol Inflamm* **1987** ; 8 : 49-53.
- [8] Selcuk E, Gomel M, Apaydin S, Kose T, Tuglular I. *Int J Clin Pharmacol Res*, **1998** 18 (1) : 21-9.
- [9] Alpaslan C, Alpaslan G, Ugar D. *J Marmara Univ Dent Fac*, **1997** Sep 2 (4) : 685-64.
- [10] Negm MM. *Oral Surg Oral Med Oral Pathol* **1989** ; 67 (1) : 88-95.
- [11] Rohde J, Schwegler F, Standel W. *Dtsch Med Wochenschr* **1980** Nov 14 ; 105 (46) : 1614-7 Eandi M, della Pepa C, Rubinato MP. *Clin Ther* **1991** ; 136(2) : 106-35s.
- [12] Eandi M, della Pepa c, Rubinato MP. *Clin Ther* **1991** : 136 (2) : 106-35.
- [13] Parfitt K. Martindale : the Complete Drug reference. 32<sup>nd</sup> edition **1999**; London: Pharmaceutical Press : 80.
- [14] Giercksey KE. *Am J Med* **1986**; 81(suppl 5 B): 2-5.
- [15] Englert R, Fontanesi G, Muller P, Ott H, Rehn L, Silva h. *Clin Ther* **1996** Sep-Oct; 18(5): 843-52.