



## Comparative Evaluation of Diclofenac Tablet, Gel, and Transdermal Patch for Postoperative Pain Management Following Third Molar Extraction: A Randomized Clinical Trial

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### KEYWORDS

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### ABSTRACT:

**Background:** Effective postoperative pain management is essential following third molar extractions. Diclofenac, a commonly used NSAID, is available in various formulations with differing pharmacokinetics and tolerability. This study compares the efficacy of oral tablets, soft gelatin capsules, and transdermal patches of diclofenac in managing postoperative pain.

**Materials and Methods:** A prospective, randomized clinical trial was conducted with 75 patients undergoing mandibular third molar extraction. Patients were divided into three groups: Group A (diclofenac transdermal patch 100 mg), Group B (oral diclofenac tablet 50 mg), and Group C (diclofenac soft gel capsule 50 mg). Pain intensity was evaluated using the Visual Analog Scale (VAS) and Verbal Rating Scale (VRS) on days 1, 2, 3, 5, and 7 postoperatively. The number of paracetamol tablets used as rescue analgesia was recorded.

**Results:** The diclofenac transdermal patch group demonstrated significantly lower VAS and VRS scores at 3 hours ( $p < 0.001$ ) and on day 3 ( $p < 0.001$ ), compared to other groups. By day 7, all groups showed similar pain relief. The patch group required fewer rescue analgesics and exhibited an earlier and more sustained reduction in pain intensity.

**Conclusion:** Diclofenac transdermal patches provide superior early postoperative pain control compared to tablets and soft gel capsules. Their non-invasive nature, better compliance, and steady drug release make them a preferable alternative in postoperative dental pain management.



## Introduction

Pain management remains a cornerstone of the postoperative recovery process, with untreated pain posing significant risks to both physical and psychological well-being. Poorly controlled postoperative pain can diminish quality of life and elevate the risk of complications, including increased morbidity and mortality.<sup>1</sup>

Defined by the International Association for the Study of Pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage,” pain is a complex and multifaceted phenomenon.<sup>2</sup> Following surgical tissue injury, changes in the somatosensory system heighten the sensitivity of central and peripheral pain pathways, necessitating strategic approaches to pain control.<sup>3</sup>

One such strategy is preemptive analgesia, which involves administering analgesics before the onset of painful stimuli. This approach aims to prevent central sensitization, offering more effective pain relief than treatment initiated after the onset of pain.<sup>4</sup> Among the medications commonly used in dental and surgical settings, nonsteroidal anti-inflammatory drugs (NSAIDs) like diclofenac are widely prescribed.<sup>5</sup> However, the oral administration of diclofenac presents limitations, including reduced bioavailability and gastrointestinal side effects due to first-pass metabolism.<sup>6,7</sup>

To overcome these challenges, novel drug delivery systems have been developed. Diclofenac potassium soft gelatin capsules offer rapid onset of action and improved patient compliance,<sup>8</sup> while transdermal patches provide a non-invasive, sustained, and controlled method of drug delivery. These patches bypass the gastrointestinal tract and first-pass metabolism, reduce systemic side effects, and offer an effective alternative for patients with difficulties in oral drug intake.<sup>9</sup>

As innovations in pain management continue to evolve, transdermal systems and advanced oral formulations represent promising tools in achieving optimal postoperative outcomes with greater safety and comfort for patients.

## Materials and Methodology

This was a single-center, prospective, randomized, comparative clinical trial designed to evaluate the efficacy of three different diclofenac formulations—oral tablet, soft gel capsule, and transdermal patch—in managing postoperative pain following the extraction of impacted mandibular third molars. The study was conducted at the Department of Oral and Maxillofacial Surgery, NIMS Dental College and Hospital, Jaipur, Rajasthan. The study protocol was approved by the Institutional Ethics Committee of NIMS Dental College. Written informed consent was obtained from all participants before enrolment. A total of 75 patients meeting the inclusion criteria were selected using a convenient sampling technique and divided into three groups: Group A (transdermal diclofenac patch), Group B (oral diclofenac tablet), and Group C (diclofenac soft gel capsule), with 25 patients in each group.

### Inclusion Criteria:

- Age: 18–55 years.
- Gender: Both male and female.
- Diagnosis: Indicated for surgical extraction of impacted mandibular third molars.
- Consent: Provided informed written consent.

### Exclusion Criteria:

- Immunodeficiency disorders.
- Uncontrolled systemic diseases.
- Use of anticoagulants.
- History of peptic ulcers.



- Known hypersensitivity to diclofenac or other NSAIDs.
- Concurrent use of corticosteroids or NSAIDs.
- Uncooperative patients or those unwilling to attend follow-ups.

The medications used were diclofenac transdermal patches (100 mg), diclofenac tablets (50 mg), diclofenac soft gel capsules (50 mg), paracetamol (500 mg), ranitidine (150 mg), and amoxicillin (500 mg). Patients were briefed about their respective pain management protocol before extraction under local anesthesia.

Postoperative analgesic administration was as follows:

- Group A (Oral Diclofenac Tablet): Diclofenac sodium 50 mg TID for 3 days, with ranitidine 150 mg BID for 3 days and amoxicillin 500 mg TID for 5 days if necessary. Paracetamol 500 mg was provided as rescue analgesia.
- Group B (Transdermal Patch): A 100 mg diclofenac patch was applied 2 hours preoperatively and replaced every 24 hours for 3 days. Patients were also prescribed ranitidine and amoxicillin as needed. Paracetamol 500 mg served as rescue medication.
- Group C (Diclofenac Soft Gel Capsule): Diclofenac potassium 50 mg TID for 3 days, along with the same adjunctive medications and rescue analgesia as above.

Primary Outcome: Postoperative pain intensity measured at five time points—days 1, 2, 3, 5, and 7—using two validated scales:

- Visual Analog Scale (VAS): A 10 cm scale from 0 (no pain) to 10 (worst pain imaginable).

- Verbal Rating Scale (VRS): A 4-point ordinal scale: 0 = Comfortable, 1 = Mild, 2 = Moderate, 3 = Severe.

Secondary Outcome: Number of paracetamol tablets consumed as rescue analgesia.

Participants were instructed to stop scoring pain after consuming rescue medication. The number of rescue tablets used was recorded for each participant.

## Result

The study compared the efficacy of Diclofenac Tablet, Patch, and Gel in managing post-operative pain, assessing pain levels using the VAS and VRS scores at multiple time points (1 hour, 2 hours, 3 hours, 3rd day, and 7th day).

At 1 hour, VAS scores were similar across all groups ( $p = 0.213$ ). At 2 hours, the Diclofenac Patch group had the lowest VAS score ( $0.84 \pm 0.94$ ) compared to the Tablet ( $1.56 \pm 1.08$ ) and Gel ( $1.24 \pm 1.09$ ) groups, though not statistically significant ( $p = 0.056$ ). At 3 hours, the Patch group had significantly lower pain scores ( $2.12 \pm 0.73$ ) compared to the Gel ( $3.52 \pm 1.23$ ) and Tablet ( $3.44 \pm 1.16$ ) groups ( $p < 0.001$ ). By the 3rd day, the Patch group maintained the lowest pain scores ( $0.36 \pm 0.57$ ) compared to the Tablet ( $1.44 \pm 1.16$ ) and Gel ( $1.52 \pm 1.23$ ) groups ( $p < 0.001$ ). By 7th day, pain was minimal in all groups with no significant difference ( $p = 0.056$ ) (Table 1 Graph 1).

The VRS scores showed significant differences at 1 hour ( $p = 0.012$ ), with the Patch group having the lowest score ( $0.12 \pm 0.33$ ). At 2 hours, the Patch group reported the lowest pain ( $0.00 \pm 0.00$ ), with a significant difference ( $p = 0.004$ ). At 3 hours, the Patch group ( $0.36 \pm 0.49$ ) had significantly lower scores than the Tablet ( $1.24 \pm 0.60$ ) and Gel ( $1.00 \pm 0.71$ ) groups ( $p < 0.001$ ). By the 3rd day, there was no significant difference ( $p = 0.743$ ), and by the 7th day, all groups reported complete pain relief ( $p = 1.000$ ) (Table 2 Graph 2).



Pain reduction was analyzed using Friedman's test. Between 1 hour and 2 hours, significant pain reduction was observed in the Patch ( $p = 0.023$ ) and Gel ( $p = 0.009$ ) groups, while the Tablet group showed a slower onset ( $p = 0.304$ ). At 3 hours, all groups exhibited significant pain reduction ( $p < 0.001$  for Tablet and Gel;  $p = 0.02$  for Patch), with the Patch group having the lowest VAS score. Between 1 hour and the 3rd day, the Patch group showed the most significant pain reduction ( $p < 0.001$ ), whereas the Tablet ( $p = 0.166$ ) and Gel ( $p = 0.140$ ) groups showed slower pain relief. By 7th day, pain relief was significant across all groups ( $p < 0.001$ ), indicating progressive improvement.

From 3 hours to the 3rd day, all groups experienced significant pain reduction ( $p < 0.001$ ). However, between 3rd and 7th day, the Tablet ( $p = 0.032$ ) and Gel ( $p < 0.001$ ) groups continued to show pain reduction, while the Patch group ( $p = 0.371$ ) did not, indicating its maximum effect was reached by the 3rd day. (Table 1)

Within-group VRS score analysis showed no significant reduction in pain between 1 hour and 2 hours ( $p > 0.05$ ). By 3 hours, significant pain reduction was observed in the Tablet ( $p < 0.001$ ) and Gel ( $p = 0.002$ ) groups, but not in the Patch group ( $p = 0.180$ ), suggesting subjective pain relief occurred slightly later in the Patch group. Between 3 hours and the 3rd day, significant reductions were observed in the Tablet ( $p < 0.001$ ) and Gel ( $p < 0.001$ ) groups, but not in the Patch group ( $p = 0.655$ ), confirming that the Patch had already reached its maximum effect. By 7th day, pain relief was significant across all groups ( $p < 0.001$  for Tablet and Gel;  $p = 0.044$  for Patch). No significant changes were noted between 3rd and 7th day ( $p > 0.05$ ), indicating that most pain relief had already occurred by the 3rd day. (Table 2)

	Group 1	Group 2	Group 3 (Diclofenac Gel)	P value <sup>a</sup>

	(Diclofenac tablet) (N=25)	(Diclofenac Patch) (N=25)	(N=25)	
VAS 1 hr	1.84±1.21	1.40±1.00	1.92±1.11	0.213
VAS 2 hr	1.56±1.08	0.84±0.94	1.24±1.09	0.056
VAS 3 hr	3.44±1.16	2.12±0.73	3.52±1.23	<0.001*
VAS 3 <sup>rd</sup> day	1.44±1.16	0.36±0.57	1.52±1.23	<0.001*
VAS 7 <sup>th</sup> day	0.20±0.41	0.00±0.00	0.20±0.41	0.056
VRS 1 hr	0.56±0.65	0.12±0.33	0.36±0.49	0.012*
VRS 2 hr	0.36±0.49	0.00±0.00	0.20±0.41	0.004*
VRS 3 hr	1.24±0.60	0.36±0.49	1.00±0.71	<0.001*
VRS 3 <sup>rd</sup> day	0.40±0.58	0.28±0.46	0.32±0.63	0.743
VRS 7 <sup>th</sup> day	0.00±0.00	0.00±0.00	0.00±0.00	1.000

a = ANOVA test, \* = Statistically significant

Table 1 Comparison of mean VAS and VRS Scores among three groups



	Group 1 (Diclofenac tablet) (N=25)	Group 2 (Diclofenac Patch) (N=25)	Group 3 (Diclofenac Gel) (N=25)
VAS 1 hr vs VAS 2 hr	0.304	0.023*	0.009*
VAS 1 hr vs VAS 3 hr	<0.001*	0.02*	<0.001*
VAS 1 hr vs VAS 3 <sup>rd</sup> day	0.166	<0.001*	0.140
VAS 1 hr vs VAS 7 <sup>th</sup> day	<0.001*	<0.001*	<0.001*
VAS 2 hr vs VAS 3 hr	<0.001*	<0.001*	<0.001*
VAS 2 hr vs VAS 3 <sup>rd</sup> day	0.721	0.152	0.264
VAS 2 hr vs VAS 7 <sup>th</sup> day	0.009*	0.02*	0.025*
VAS 3 hr vs VAS 3 <sup>rd</sup> day	<0.001*	<0.001*	<0.001*
VAS 3hr vs	<0.001*	<0.001*	<0.001*

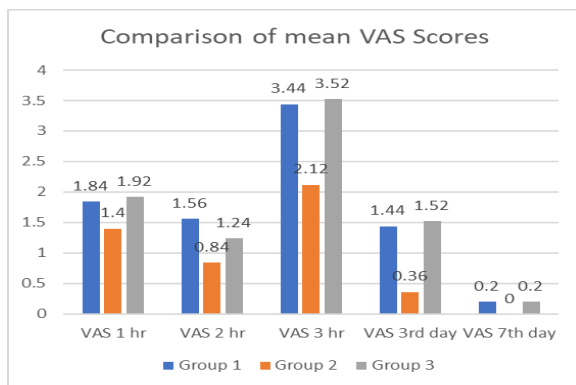
VAS 7 <sup>th</sup> day			
VAS 3 <sup>rd</sup> day vs VAS 7 <sup>th</sup> day	0.032*	0.371	<0.001*
VRS 1 hr vs VRS 2 hr	0.325	0.502	0.348
VRS 1 hr vs VRS 3 hr	<0.001*	0.180	0.002*
VRS 1 hr vs VRS 3 <sup>rd</sup> day	0.395	0.371	0.655
VRS 1 hr vs VRS 7 <sup>th</sup> day	0.009*	0.502	0.081
VRS 2 hr vs VRS 3 hr	<0.001*	0.044*	<0.001*
VRS 2 hr vs VRS 3 <sup>rd</sup> day	0.893	0.118	0.623
VRS 2 hr vs VRS 7 <sup>th</sup> day	0.107	1.00	0.421
VRS 3 hr vs	<0.001*	0.655	<0.001*



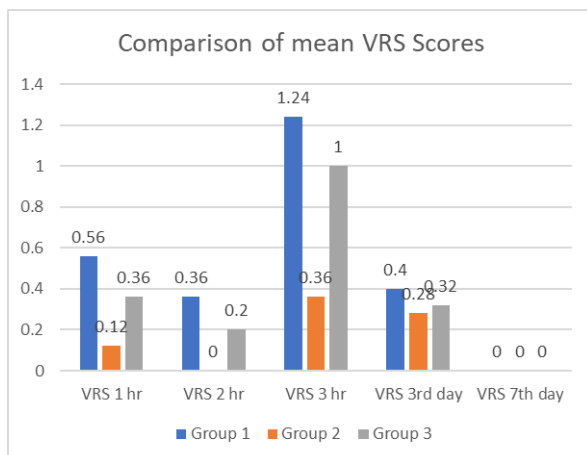
VRS 3 <sup>rd</sup> day			
VRS 3hr vs VRS 7 <sup>th</sup> day	<0.001*	0.044*	<0.001*
VRS 3 <sup>rd</sup> day vs VRS 7 <sup>th</sup> day	0.081	0.118	0.195

\* = Statistically significant

Table 2 Pairwise comparison for VAS and VRS among three groups using Friedman’s test



Graph 1 shows the comparison of mean VAS scores among three groups



Graph 2 shows the comparison of mean VRS scores among three groups

### Discussion

People usually link dental care with pain, and when dental pain is not adequately controlled, it can make patients more difficult to treat and cause them to put off or delay treatment.<sup>[10]</sup>

An important aspect of oral and maxillofacial surgery is the extraction of third molars. While anesthesia must be administered during removal, adequate postoperative analgesia is just as crucial for patient care.<sup>[11]</sup>

Third molar impaction is a prevalent condition that frequently calls for its extraction <sup>[12]</sup>. A popular model for evaluating the effectiveness of analgesics for acute dental pain is the surgical extraction of an impacted third molar.<sup>[10]</sup>

It is often known that the discomfort experienced following the extraction of third molars is brief and peaks in the early postoperative phase <sup>[12]</sup>. Following third molar surgery, the majority of young, healthy adults can anticipate experiencing mild discomfort and activity limitations for no more than five days. Pain should gradually subside throughout the first five days following surgery, and disruptions to regular activities, employment, and education should be limited to the first three days. <sup>[13]</sup>.

One of the most widely used analgesics for post-operative dental pain is non-steroidal anti-inflammatory drugs, or NSAIDs. Inhibiting cyclooxygenases 1 and 2 (COX-1 and COX-2), important enzymes in prostaglandin (PG) formation, is a major factor in NSAIDs' ability to reduce pain.<sup>14</sup>

For NSAIDs, transdermal delivery systems are a cutting-edge alternative to oral and other conventional drug administration methods. The transdermal patch's medication diffuses into capillaries for systemic distribution after entering the body through the skin. The continuous penetration of medicine across the skin provides for more stable serum drug levels, generally an objective of therapy <sup>15,16</sup>



For post-tooth extraction pain, a transdermal diclofenac patch containing 100 mg applied once day proved to be just as effective as oral diclofenac 150 mg daily. These results are comparable to those of Funk et al. [17], who found that oral and transdermal diclofenac had comparable analgesic efficacy in treating patients with post-operative shoulder pain. After laparoscopic surgery, diclofenac patches have also been shown to offer effective analgesia. [18]

Mason et al.'s [19] systematic evaluation of topical NSAID use in the UK and studies detailing the use of the diclofenac transdermal patch for osteoarthritis [20] and sports-related injuries have further highlighted the safety profile of diclofenac patches. [21]

The concept behind the new technology, called ProSorb (aaiPharma Inc., Wilmington, NC), is the use of specific dispersing agents that are intended to facilitate more rapid, consistent, and complete absorption of NSAIDs from the GI tract. Diclofenac sodium softgel was the novel softgel formulation of diclofenac sodium created using the ProSorb technology. Most NSAIDs precipitate upon exposure to gastric fluid due to their relative insolubility at acidic pH, and absorption characteristics rely on mechanical agitation to disperse the drug in the stomach, which may lead to unreliable and highly variable absorption between individuals after oral administration. [22]

According to this early research, the softgel formulation of diclofenac sodium causes far quicker absorption of the medication from the gastrointestinal tract than Cataflam. The study was therefore guided by the hypothesis that, when used to treat acute painful conditions, diclofenac sodium softgel would produce analgesia more quickly and possibly for a longer period of time than an equivalent dose of conventionally formulated diclofenac due to its faster absorption of diclofenac anion. [22]

Although measuring pain is subjective by nature, there are a number of scales that can be used, such as the visual Analog Scale, Verbal Rating Scale, Pain Intensity Scale, and Pain Relief Scale. The 11-point Visual Analog Scale goes from 0 (no discomfort) to 10 (highest agony). Similarly, the Verbal Rating Scale is a shorter, 4-point scale (0-3), indicating pain levels from "no pain" to "severe pain."

This comparative interventional study assesses how well Diclofenac tablets, transdermal patches, and gel work to treat patients' postoperative pain. This study design helps minimize bias. The Visual Analog Scale (VAS) and Verbal Rating Scale (VRS) were used to measure postoperative pain at one-, two-, three-, and seven-day intervals. Additionally, since paracetamol 650 mg was used as an emergency medication, the number of tablets consumed by each patient was recorded.

At the 1-hour mark, the Visual Analog Scale (VAS) scores were comparable across all groups, indicating no significant difference in the immediate analgesic effect among the three formulations.

However, at 2 hours, the Diclofenac Patch group exhibited lower VAS scores than the Tablet and Gel groups, suggesting a potential early onset of pain relief with the transdermal formulation. Although there was no significance difference. ( $p = 0.056$ ), The pattern shows a possible advantage of the patch in providing sustained pain relief over time.

A significant difference in pain levels emerged at 3 hours ( $p < 0.001$ ), where the Diclofenac Patch group reported the lowest VAS scores ( $2.12 \pm 0.73$ ) compared to the Gel ( $3.52 \pm 1.23$ ) and Tablet ( $3.44 \pm 1.16$ ) groups. This suggests that the transdermal route may offer a more prolonged and effective analgesic effect, likely due to its ability to maintain steady plasma drug



concentrations while bypassing gastrointestinal metabolism.

By the 3rd day, the Diclofenac Patch continued to show superior pain control ( $0.36 \pm 0.57$ ) compared to the Tablet ( $1.44 \pm 1.16$ ) and Gel ( $1.52 \pm 1.23$ ) groups with significance variation ( $p < 0.001$ ). This further supports the sustained-release benefit of the patch formulation, which may contribute to better patient compliance and reduced need for additional analgesic interventions. By the 7th day, pain levels were minimal across all groups, with no statistically significant difference ( $p = 0.056$ ), indicating effective overall pain resolution regardless of the Diclofenac formulation used. This suggests that while early postoperative pain management varies between formulations, long-term outcomes remain comparable. This outcome was consistent with the findings of Bhaskar et al. (2010)<sup>23</sup>, who demonstrated that the mean pain score decreased over time in both groups when comparing post-operative pain.

The comparison of mean Verbal Rating Scale (VRS) scores at different time points further supports the superior effect of the Diclofenac transdermal patch in postoperative pain management. At the 1-hour mark, a significance difference was observed ( $p = 0.012$ ), with the Diclofenac Patch group reporting the lowest pain scores ( $0.12 \pm 0.33$ ) compared to the Tablet ( $0.56 \pm 0.65$ ) and Gel ( $0.36 \pm 0.49$ ) groups. This early reduction in pain suggests that the transdermal formulation provides a more effective initial analgesic response.

At 2 hours, the VRS scores continued to demonstrate a statistically significant difference ( $p = 0.004$ ), with the Diclofenac Patch group reporting no pain ( $0.00 \pm 0.00$ ), whereas the Tablet and Gel groups showed higher scores. This finding highlights the potential of the transdermal patch to achieve faster pain relief, likely due to its steady drug absorption and prolonged therapeutic effect.

By the 3-hour mark, the Diclofenac Patch remained the most effective formulation, with significantly lower pain scores ( $0.36 \pm 0.49$ ) compared to the Tablet ( $1.24 \pm 0.60$ ) and Gel ( $1.00 \pm 0.71$ ) groups ( $p < 0.001$ ). This reinforces the earlier findings from the VAS assessment, indicating that the patch provides sustained pain relief and may be a preferred alternative to oral and topical formulations.

By the 3rd day, there was no difference between groups ( $p = 0.743$ ), suggesting that all formulations contributed to adequate long-term pain management. By the 7th day, complete pain relief was achieved in all groups, as reflected by a VRS score of 0 across all participants ( $p = 1.000$ ). This result contradicts to Bachalli PS et al. (2009)<sup>7</sup>

The onset of analgesia for diclofenac sodium softgel was as rapid as that after parenteral administration of diclofenac sodium, faster than that after an equivalent dose of diclofenac in Cataflam, and faster than those described for typical dosages of other NSAIDs<sup>24-28</sup>. There was no statistically significant difference in rescue measures between the two active formulation groups, indicating a comparable duration of effect.

These results align with the trends observed in the VAS analysis, further confirming that the Diclofenac transdermal patch provides superior pain control in the early postoperative period. The findings suggest that transdermal drug delivery may offer an effective, non-invasive, and patient-friendly alternative to oral and topical Diclofenac formulations.

### Limitations:

- Small sample size ( $n = 75$ ), limiting generalizability.
- Pain perception is subjective and could be influenced by individual thresholds and expectations.



## Conclusion

The Diclofenac transdermal patch proved to be a superior option for postoperative pain management, offering faster and sustained relief compared to tablets and gel. It provided significantly lower VAS and VRS scores at early time points due to steady drug levels and bypassing gastrointestinal metabolism. Although pain relief was similar across groups by day 7, the patch ensured better early control and reduced additional analgesic use. Its non-invasive nature and minimal side effects make it a promising alternative for future pain management

## Abbreviations

VAS	Visual Analog Scale
VRS	Verbal Rating Scale
NSAIDs	Nonsteroidal Anti-inflammatory Drugs
TID	Ter in Die (three times a day)
BID	Bis in Die (twice a day)
mg	Milligrams
ANOVA	Analysis of Variance
SD	Standard Deviation

## Clinical Significance

This study demonstrates that the diclofenac transdermal patch offers an effective and patient-friendly alternative for early postoperative pain control following third molar surgery. Its ability to bypass the gastrointestinal system reduces systemic side effects and enhances compliance. These findings support the integration of transdermal drug delivery systems into routine dental pain management protocols, especially for patients with contraindications to oral NSAIDs or compliance challenges.

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