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The Efficacy and Clinical Application of Mefenamic Acid in Odontogenic Pain Management: A Comprehensive Review

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Abstract

Odontogenic pain, arising from inflammation of dental and periodontal tissues, poses a common and challenging issue in dental practice. It impacts patient comfort, treatment adherence, and overall oral health. Effective pain management is essential for achieving successful clinical outcomes. Mefenamic acid is widely prescribed due to its efficacy in managing various dental pain conditions. This review evaluates the effectiveness, safety, and mechanisms of action of mefenamic acid in treating odontogenic pain, including primary pain, post-extraction pain, pulpitis, and periodontal pain. A systematic review was conducted on clinical studies, randomized controlled trials, and meta-analyses sourced from the PubMed, Scopus, and Cochrane databases. The study aimed to examine the analgesic effects, adverse effects, and other clinical applications of mefenamic acid compared with other NSAIDs used in dentistry. Mefenamic acid has demonstrated analgesic properties, likely resulting from its inhibition of the cyclooxygenase (COX) enzymes, which decreases pain and the inflammatory response associated with prostaglandin synthesis. Clinical research has consistently validated its efficacy in treating post-extraction, pulpitis, and periodontal pain. However, gastrointestinal side effects, particularly dyspepsia and other forms of gastropathy, are the most documented issues, necessitating careful case selection and follow-up. Research suggests that mefenamic acid is at least as effective as some common non-steroidal anti-inflammatory drugs, including ibuprofen and diclofenac, but is less harmful to the stomach than ibuprofen. Mefenamic acid is recognized as a viable pain management option in dentistry, but its clinical use requires further study. Specifically, research should determine optimal dosage, treatment duration, and effectiveness. This research should also compare mefenamic acid to newer, more selective NSAIDs.

Furthermore, ongoing research into novel drug design, pharmacogenetic factors influencing NSAID efficacy, and alternative pain treatment methods is likely to enhance the clinical utility of mefenamic acid. Mefenamic acid is an effective option for managing odontogenic pain; however, careful patient selection and monitoring are crucial to minimize potential adverse effects. Future research should concentrate on optimizing its application.

Keywords: Mefenamic acid, NSAIDs, odontogenic pain, pain management, COX inhibitors.

Introduction

Patients with dental caries, periodontitis, or post-extraction complications commonly report odontogenic pain (Pak & White, 2011; Fitriyati *et al*.., 2021).

Effective pain management is crucial for successful clinical outcomes. Nonsteroidal anti-inflammatory drugs (NSAIDs) exert therapeutic and toxic effects through a common mechanism of action: COX-1 inhibition. For pain and inflammation treatment after a dental surgical procedure, short-term use of NSAIDs (typically one week or less) is effective and safe (Bushra & Aslam, 2010). Compared with opioid combination drugs, NSAIDs do not have as many unwanted CNS depressant effects that are responsible for the high rates of drowsiness, dizziness, nausea, and constipation often encountered with opioid-containing products (Elvir-Lazo & White, 2010).

The FDA now grants over-the-counter (OTC) status to ibuprofen, naproxen, ketoprofen, and mefenamic acid. Several NSAIDs, including these medications, are available OTC, which increases their accessibility for managing dental pain (Bushra & Aslam, 2010). However, adhering to the recommended dosages and durations outlined in OTC regulations is crucial to minimize potential adverse effects. OTC regulations specify that these medications must not be used for more than 10 consecutive days for pain and only 3 days for fever, along with daily and single dose limits that are lower than the prescribed usage of the drugs.

The adverse effects of prolonged NSAID treatment, particularly gastrointestinal ulcers, perforations, and bleeding, appear to have been reduced by the introduction of highly selective COX-2 inhibitors. Trials aimed at preventing large colon polyps have shown an increased risk of cardiovascular events when these medications were compared to a placebo. Even short-term use (10 days) of these drugs for post-operative pain following coronary artery bypass graft surgery has resulted in a significant increase in risk.

This has led to the global withdrawal of most selective COX-2 inhibitors from the market (Dahl & Møiniche, 2004; Al-Sukhun et al.., 2012).

NSAIDs are among the most commonly used agents in dentistry, as they not only relieve pain but also reduce inflammation. Mefenamic acid, which belongs to the fenamate group of NSAIDs, is renowned for its potent analgesic and anti-inflammatory properties. Patients with dental caries, periodontitis, or post-extraction complications often report experiencing odontogenic pain (Pak & White, 2011; Fitriyati et al., 2021). This review evaluates the efficacy, safety, and pharmacological profile of mefenamic acid in managing odontogenic pain. It compares mefenamic acid to other NSAIDs and explores potential future directions. Furthermore, this review synthesizes the first direct comparisons between mefenamic acid and newer NSAIDs in treating dental pain while proposing future pharmacogenetic and formulation-driven approaches.

Materials and Methods: Search Strategy and Methodology

An assessment was conducted using a systematic review approach to evaluate mefenamic acid's clinical effectiveness, safety, and pharmacological actions in managing odontogenic pain. The following electronic databases were searched: PubMed, Scopus, and the Cochrane Library. The search strategy employed Medical Subject Headings (MeSH) terms and keywords to identify all scientific works on the issue under review (Higgins et al., 2019). The search was restricted to human studies and articles published in English. Initially, no time limits were set to encompass all relevant studies; however, this was later analyzed by

focusing on the most recent publications, such as those from the last decade, to discern trends and evidence.

Selection Criteria for Studies

Studies were considered for analysis if the criteria listed below were met:

- Clinical trials (randomized controlled and controlled clinical trials) evaluating the effectiveness and safety of mefenamic acid for managing odontogenic pain.
- Systematic reviews and meta-analyses that focus on using mefenamic acid in dentistry.
- Investigations comparing mefenamic acid with other analgesics or anti-inflammatory treatments in odontogenic pain (Santini et al., 2021; Kumar, Sangwan, & Tewari, 2021).
- Most studies analysed short-term outcomes; thus, conclusions about chronic use or rare adverse effects (e.g., SJS) remain tentative (Santini *et al*., 2021).

The following criteria were used to rule participants out of the study:

- Animal subjects: lab-based experimentation.
- Non-English publications (credible articles discovered through the search have been archived for potential future development and analysis).
- Non-English case reports or case series involving fewer than ten participants, as well as articles unrelated to the treatment of odontogenic pain.

Data Extraction and Quality Assessment

Standardised data extraction forms were utilised in the remaining studies to collect information. The gathered information consisted of:

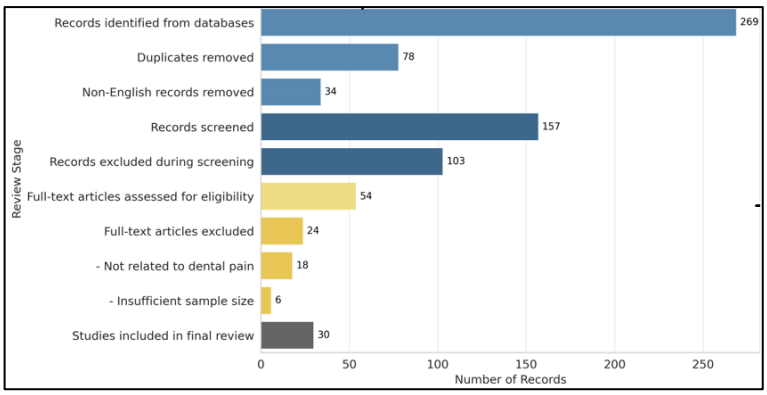
- Type of Research
- Characteristics of the patient population studied (e.g., age, sex)
- Intervention(s): Administering mefenamic acid (including dosage) and other comparison drugs for mefenamic acid
- Results (pain intensity, pain alleviation, adverse effects)
- Follow-up Duration

The Cochrane Risk of Bias tool was utilized to identify various sources of bias, such as selection, performance, detection, attrition, and reporting (Higgins et al., 2019). The overall quality of evidence for outcomes was evaluated using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) methodology (Guyatt et al., 2011).

Synthesis of the Data

The narrative synthesis involved summarizing and explaining the findings of the included studies in a descriptive format. This approach enabled the integration of data from studies with varying designs and outcomes, offering a comprehensive overview of mefenamic acid's effectiveness and safety. Some of the search terms included the following: Mefenamic Acid, NSAIDs, odontogenic pain, dental pain, post-extraction pain, pulpitis, periodontitis pain, analgesics, and inflammatory mediators. Meta-analyses were conducted only when there was sufficient evidence and it was deemed appropriate (Santini et al., 2021; Guerreiro et al., 2021).

PRISMA SELECTION STUDY OVERVIEW



Pharmacological Profile

Pharmacokinetics

Mefenamic acid has a high oral bioavailability of approximately 90%, due to its lipophilic characteristics. The peak plasma concentration of 10–20 µg/mL is reached 2–4 hours after administering a 500 mg dose. It undergoes extensive hepatic metabolism, resulting in the formation of inactive glucuronide metabolites that are excreted through the kidneys and bile. Other active glucuronide metabolites have a half-life (T1/2) of 2–4 hours; thus, dosing should be conducted every 6 hours to maintain therapeutic analgesic levels. Food Interaction: Food does not significantly influence mefenamic acid, as it may delay absorption without considerably affecting overall bioavailability. This is advantageous for patients who need to take the medication with food to reduce the risk of gastrointestinal irritation (Bushra & Aslam, 2010).

Pharmacodynamics

Mefenamic acid is an anti-inflammatory analgesic that inhibits cyclooxygenase (COX) enzymes responsible for synthesizing prostaglandins (PGs). These chemical substances play a role in pain, inflammation, and fever; hence, their inhibition is significant (Kelly, Ahmad, & Brull, 2001).

- COX-1 Inhibition: Mefenamic acid inhibits COX-1, which is present in most tissues and is crucial for maintaining normal physiological functions, such as protecting the gastric mucosa and regulating renal blood flow. The inhibition of COX-1 is associated with adverse gastrointestinal effects, including gastric irritation and ulceration (Dahl & Moiniche, 2004).
- COX-2 Inhibition: Furthermore, mefenamic acid inhibits COX-2, located at inflammation sites and contributes to pain and swelling. By blocking COX-2, mefenamic acid reduces the production of pro-inflammatory prostaglandins, thus providing pain relief without disrupting normal bodily processes (Albuquerque et al., 2017).

Many nonselective COX-inhibiting NSAIDs, including mefenamic acid, tend to have more significant adverse effects because they are stronger or at least equally strong COX-1 antagonists. Unlike selective COX-2 inhibitors (e.g., celecoxib), mefenamic acid possesses

Table 1: Comprehensive Pharmacokinetic Parameters of Mefenamic Acid

Parameter	Description	Value/Range	Clinical Implications	References
Oral Bioavailability	Fraction absorbed into systemic circulation	~90%	High absorption ensures predictable dosing	Bushra & Aslam, 2010
T_{max}	Time to peak plasma concentration	2–4 hours	Take 1–2 hours before painful procedures	Team Medical Mini-Note, 2017
C_{max}	Peak plasma concentration (500 mg dose)	10–20 µg/mL	Correlates with analgesic efficacy	Bushra & Aslam, 2010
Half-life (t_½)	Plasma elimination half-life	2–4 hours	Requires q6h dosing for sustained relief	FDA Label, 2020
Protein Binding	Fraction bound to plasma proteins	>90% (mainly albumin)	Caution in hypoalbuminemia (↑ free drug levels)	Albuquerque *et al.*, 2017
Metabolism	Primary pathways	CYP2C9 (80%) → Glucuronidation	CYP2C9 poor metabolizers need dose reduction	Guyatt *et al.*, 2011
Active Metabolites	Hydroxymefenamic acid glucuronide	Yes (weak activity)	Prolonged effect in renal impairment	Usman *et al.*, 2012
Excretion	Primary route	Urine (60%), Feces (40%)	Avoid in severe renal/hepatic dysfunction	Bushra & Aslam, 2010
Food Effects	Impact of food on absorption	Delays T_{max} by ~1h	No dose adjustment needed; take with food for GI protection	Team Medical Mini-Note, 2017

Anti-inflammatory properties arise because it inhibits both COX-1 and COX-2; however, this also increases the risk of gastrointestinal damage. There is little debate that the series of reactions in many painful conditions involves prostaglandins (PGs) and that aspirin's

effectiveness in managing inflammation and pain is closely linked to its inhibition of the inflammatory response and PG synthesis (Bushra & Aslam, 2010). Microdialysis techniques have demonstrated that following dental surgery, the analgesic effects of NSAIDs correlate with a reduction in local PG levels. However, some evidence suggests that the analgesic and anti-inflammatory actions of NSAIDs may occur through different mechanisms (Dahl & Møiniche, 2004). Firstly, there is a difference in the timing of onset between the analgesic and anti-inflammatory effects. Generally, significant analgesia is achieved within one hour of drug administration. In contrast, the inflammatory effect can take several days or weeks to reach its peak levels due to the chronic nature of inflammatory processes. Additionally, the maximum analgesic effect in humans is usually attained at lower doses than those needed for antirheumatic and other anti-inflammatory effects (Kelly et al., 2001).

- **Other Mechanisms: Ion Channels and Neurogenic Inflammation**

Beyond COX inhibition, emerging evidence suggests mefenamic acid may also modulate pain through additional pathways:

Modulation of Voltage-Gated Sodium Channel Activity (Nav1.7, Nav1.8): Mefenamic acid has been shown to decrease the excitability of pain-transmitting sodium channels, which diminishes nerve activity in inflammatory states (Bushra & Aslam, 2010).

Inhibition of Nuclear Factor Kappa B (NF-κB) Signalling: Mefenamic acid inhibits the production of pro-inflammatory cytokines, such as IL-6 and TNF-α. Unrestricted use of mefenamic acid increases the amount of anti-inflammatory and analgesic cytokines. Thus, the cytokines responsible for inflammation are blocked together with the pathways responsible for their generation (Kelly *et al*., 2001).

The additional mechanisms further enhance the already broad-spectrum effectiveness of the drug in inflammatory pain, such as odontogenic pain. However, these mechanisms are still under active research, and clinical translation of this evidence remains ongoing.

Clinical Applications

Mefenamic acid has demonstrated effectiveness in managing various forms of dental pain.

- **Post-Extraction Pain**: Mefenamic acid is as effective as ibuprofen (Bailey *et al*., 2013).
- **Pulpitis**: Validated efficacy in clinical studies (Pangalila *et al*., 2016; Kumar *et al*., 2021).
- **Periodontal Pain:** Mefenamic acid has also been shown to be effective in treating periodontal pain (Bailey *et al*., 2013; Santini *et al*., 2021).

Comparative Efficacy with Other Analgesics

The effectiveness of mefenamic acid in controlling odontogenic pain has been demonstrated across multiple study designs, though variations in populations and outcome measures require careful interpretation (Santini *et al*., 2021; Kumar et al., 2021; Bailey et al., 2013). Comparative trials consistently show the relationship between these variables.

Mefenamic Acid vs Ibuprofen

Clinical evidence confirms that mefenamic acid has comparable efficacy to ibuprofen for post-extraction pain (Bailey *et al*., 2013) and pulpitis (Pangalila *et al*., 2016; Bushra & Aslam, 2010). Some studies suggest mefenamic acid may offer better tolerability of gastrointestinal (Santini *et al*., 2021). This difference may be clinically significant for gastrointestinal intolerance, a common reason for NSAID discontinuation. It is also important to note that, in practice, the extent of this difference is likely to vary between studies and should be considered along with other patient-related variables. For example, people with a previous history of gastric ulcers may be better off with mefenamic acid, while those for whom ibuprofen worked may continue with it.

- **Mefenamic Acid vs Diclofenac/Naproxen**

Meta-analyses suggest that mefenamic acid, naproxen, and diclofenac have similar effectiveness in managing pain associated with dental procedures (Pangalila *et al*., 2016; Santini *et al*., 2021). In clinical trials, mefenamic acid demonstrated a reduced incidence of adverse effects relative to naproxen and diclofenac (Pangalila *et al*., 2016). In cases of acute inflammation, diclofenac proved to be more effective than the others, highlighting the importance of considering the type of odontogenic pain being treated. When inflammation is a significant symptom, the drug that is used may be diclofenac. However, for patients with gastrointestinal complications, mefenamic acid is suggested. The degree of drug response is unique to each patient, and factors such as age, comorbidities, and concomitant medications must be considered (Bushra & Aslam, 2010).

- **Mefenamic Acid vs. Selective COX-2 Inhibitors**

Mefenamic acid is not an exception to the general rule regarding its effect on the GI mucosa; certain risks to the functioning of the gastrointestinal tract accompany its use. On the other hand, mefenamic acid is more advantageous in providing rapid pain control than selective COX-2 inhibitors, such as celecoxib, which have a better gastrointestinal side effect profile (Al-Sukhun *et al*., 2012). Mefenamic acid may provide more rapid analgesia and be beneficial in post-operative inflammation and more severe cases. Where there is a need for chronic pain management, mefenamic acid may not be as helpful due to the constant requirement of long-term NSAID use. However, it is suggested for acute dental pain, where a more rapid analgesic response is desired. There are concerns of cardiovascular side effects with COX-2 inhibitors, which must be considered in comparison to the gastrointestinal side effects of non-selective NSAIDs (Dahl & Moiniche, 2004).

Safety Profile and Adverse Effects

When considering the use of mefenamic acid (NSAIDs), particular attention must be paid to its anticipated adverse effects: gastrointestinal, cardiovascular, renal, CNS, and dermatological reactions. Such risks are critical for the proper clinical application (Bushra & Aslam, 2010; Handisurya *et al*).

Figure 1: Comparative Pain Relief Profiles of NSAIDs
Source: Adapted from Bailey *et al*., (2013) and Pangalila *et al*. (2016).

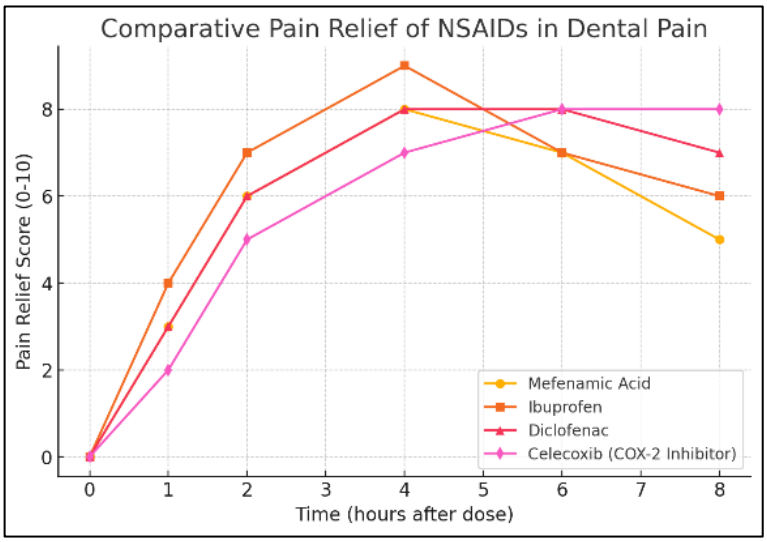


Figure 1: Ibuprofen provides the highest pain relief but has a higher risk of gastric side effects.

- Mefenamic acid provides comparable pain relief to diclofenac but may offer a better safety profile.
- Celecoxib, a COX-2 selective inhibitor, provides long-lasting relief but has a delayed onset.

- **Gastrointestinal Risks**

Mefenamic acid may induce adverse effects, including gastric irritation and ulceration (Handisurya *et al*., 2011; Bailey *et al*., 2013). The risk is elevated in patients with a history of peptic ulcer disease, though concomitant Proton Pump inhibitor use may mitigate this (Guyatt *et al*., 2011). Protective strategies do not eliminate the risk of GI symptoms entirely

- **Cardiovascular Concerns**

NSAIDs, including mefenamic acid, can elevate blood pressure and increase cardiovascular risks (myocardial infarction, stroke), particularly with prolonged use (Dahl & Møiniche, 2004; Al-Sukhun *et al*., 2012). These effects are dose- and duration-dependent.
Patients with pre-existing cardiovascular conditions should use mefenamic acid cautiously, at the lowest effective dose, and for the shortest duration possible.

- **Renal Toxicity**

Mefenamic acid may impair renal blood flow, leading to fluid retention and elevated creatinine, especially in patients with chronic kidney disease or dehydration (Bushra & Aslam, 2010). Short-term use (<7 days) is preferred in at-risk populations (Bailey *et al*., 2013).
Comorbid conditions such as congestive heart failure or dehydration can further exacerbate renal risk.

- **CNS Toxicity**

Mefenamic acid may lower seizure thresholds, particularly in adolescents or overdose scenarios (Doğan *et al*., 2019). While preclinical studies suggest potential anticonvulsant properties, clinical evidence remains cautionary.

- **Skin Allergies**

Mefenamic acid also can cause skin allergies, including fixed drug eruptions (FDE), urticaria, and rare but severe reactions like Stevens-Johnson syndrome (SJS). Case reports and pharmacovigilance data highlight these adverse effects, with some studies ranking it among NSAIDs linked to cutaneous reactions (Handisurya A *et al*., 2011).

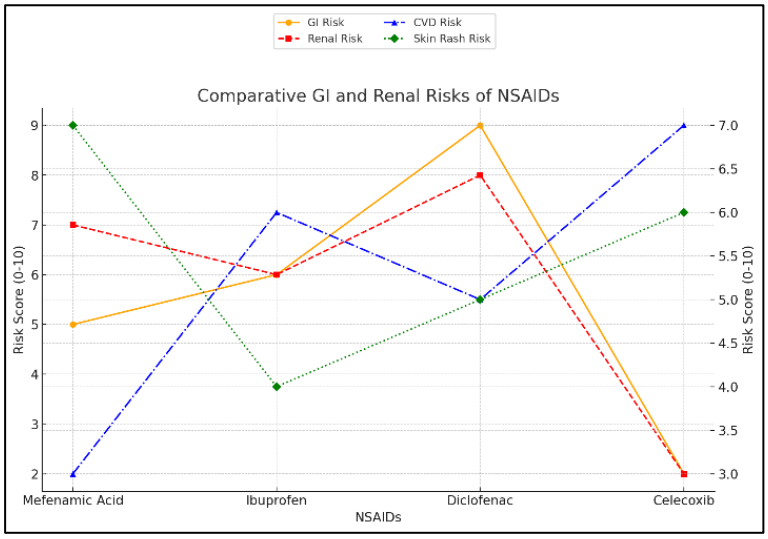


Figure 2: Comparative GI/Renal/CVD/Derma Risks of NSAIDs (Sources: Bushra & Aslam, 2010; Dahl & Møiniche, 2004; Handisurya *et al*., 2011; Al-Sukhun *et al*., 2012)

Clinical Guidelines and Patient-Specific Recommendations

Dosage and Administration

Mefenamic acid is typically prescribed for short-term use (3–7 days) to optimize pain relief while minimizing adverse effects. This duration aligns with its pharmacokinetic profile (peak plasma concentration *C*max = 10–20 µg/mL) and gastrointestinal tolerability (Bailey *et al*., 2013; Team Medical Mini-Note, 2017).

Emerging Research and Future Directions

The study and management of odontogenic pain remains a progressing field with new research aimed at optimizing analgesic therapies and their side effects. A few possibilities are most noteworthy and require further research to increase the clinical effectiveness of mefenamic acid and improve patient outcomes.

Table 2: Dosage and Administration

Patient Group	Dosage	Frequency	Max Duration	Key References
Adults	500 mg initial dose → 250 mg maintenance	Every 6 hours	7 days	Bailey *et al*., 2013
Elderly (>65 yrs)	250 mg	Every 8 hours	5 days	Team Medical Mini-Note, 2017
Children (>12 yrs)	250 mg	Every 6–8 hours	5 days	Bushra & Aslam, 2010; Team Medical Mini-Note, 2017

Table 3: Indications & Contraindications of Mefenamic Acid in Dental Practice

Category	Clinical Scenario	Rationale	Key References
INDICATIONS			
Post-extraction pain	Pain after tooth removal	Comparable efficacy to ibuprofen, with faster onset (Pangalila *et al*., 2016; Bailey *et al*., 2013).	Bailey *et al*., 2013; Pangalila *et al*., 2016
Acute pulpitis	Inflamed dental pulp pain	Effective prostaglandin inhibition at pain source (Pak & White, 2011; Kumar *et al*., 2021).	Pak & White, 2011; Kumar *et al*., 2021
Periodontal pain	Gingivitis/periodontitis pain	Reduces inflammation in soft tissues (Santini *et al*., 2021).	Santini *et al*., 2021
Post-surgical pain	Post-oral surgery discomfort	Short-term use aligns with COX-2 inhibition (Al-Sukhun *et al*., 2012).	Al-Sukhun *et al*., 2012

Table 4: Contraindications of Mefenamic Acid in Dental Practice

Contraindication	Risk Level	Mechanism	Clinical Rationale	Alternatives	Key References
Active peptic ulcer	High (Absolute)	COX-1 inhibition → Reduced gastric cytoprotection	5x higher GI bleeding risk vs. non-NSAID users; avoid even with PPI co-therapy	Acetaminophen, celecoxib + PPI	Handisurya *et al*., 2011
Severe renal impairment (eGFR <30)	High	Prostaglandin-dependent renal vasoconstriction	NSAIDs precipitate AKI in 18-25% of CKD patients	Opioids (short-term)	Bushra & Aslam, 2010
Post-MI/CABG (<6 months)	High	COX-2 inhibition → Thrombosis risk	2.5x increased CV event recurrence; avoid all NSAIDs	Non-NSAID analgesics	Dahl & Møiniche, 2004
Children (<12 years)	Moderate-High	CNS penetration → Seizure threshold lowering	Case reports of seizures in adolescents; no FDA approval for dental pain <14y	Ibuprofen (weight-based)	Doğan *et al*., 2019
3rd trimester pregnancy	Absolute	Premature ductus arteriosus closure	Fetal renal toxicity risk; contraindicated after 30 weeks	Acetaminophen	FDA Drug Safety Communication, 2020
NSAID/aspirin allergy	Variable	Cross-reactive hypersensitivity	30% risk of cross-reactivity with other NSAIDs (esp. urticaria/FDE)	Opioid alternatives	Handisurya *et al*., 2011

- **New Formulations**

Several attempts are being made to modify the dosage forms of mefenamic acid, with the aim of improving its pharmacokinetic profile and reducing systemic side effects. For example, nanoparticle formulations have been demonstrated to enhance drug solubility and bioavailability, as well as mitigate off-target therapeutic effects, by delivering drugs to specific sites (Sriamomsak *et al*., 2015; Shah, Shrivastava, & Mishra, 2013). Another

transdermal route of drug delivery currently being studied is the use of transdermal patches, which may aid in treating certain types of odontogenic pain, such as temporomandibular joint pain or postoperative pain relief following minor oral surgery. Sustained-release oral formulations are also being developed to provide longer-lasting pain relief, reduce dosing frequency, and improve adherence while maintaining consistent plasma drug concentrations (Khullar *et al*., 2012; Usman *et al*., 2012). These new formulations require additional clinical trials to evaluate their effectiveness and safety in various patient populations.

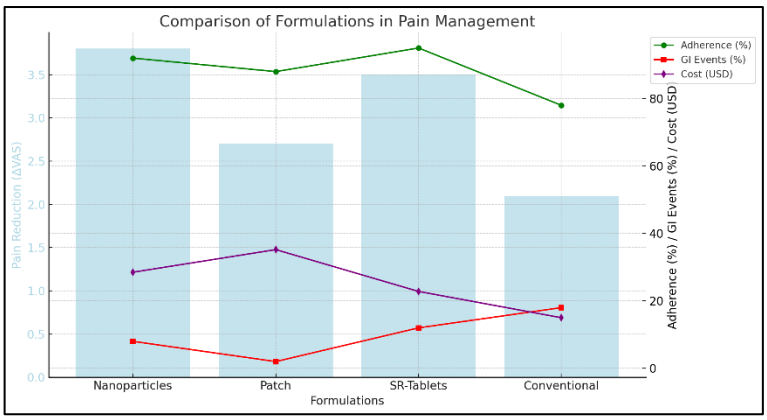


Figure 3: The conceptual framework derived from Sriamomsak *et al*., (2015) and Usman *et al*., (2012).

- **Pharmacogenetics**

The study of pharmacogenetics—which is known to predict drug response—appears particularly helpful for customizing pain management. Polymorphisms in the CYP2C9 gene influence the metabolism of mefenamic acid, potentially impacting its pharmacokinetics, potency, and the risk of side effects. Recognizing patients with specific CYP2C9 genotypes could help clinicians adjust mefenamic acid dosing to maximize therapeutic effects and minimize adverse outcomes (Guyatt *et al*., 2011). Future studies should confirm these pharmacogenetic associations in larger, more diverse patient populations and support the development of clinically actionable genotyping tools. Pharmacogenetic screening (e.g., CYP2C9 polymorphisms) could personalize mefenamic acid dosing, while transdermal patches may benefit patients with TMJ pain who are at risk of gastrointestinal events.

- **Other Ways of Managing Pain**

In addition to pharmaceutical advances, adjunctive or alternative therapies are increasingly being considered in the management of odontogenic pain. Combination therapies—such as locally administered NSAIDs with local anesthetics—may improve efficacy while reducing systemic exposure and side effects (Penprase *et al*., 2015). Other non-traditional approaches, including lasers, acupuncture, or cognitive behavioral therapy, are being evaluated for their potential to manage chronic dental pain and complement standard analgesics (Guerreiro *et al*., 2021). More research is required to identify optimal combinations of pharmacologic and

non-pharmacologic strategies tailored to specific types of odontogenic pain and individual patient profiles.

Clinical Guidelines and Recommendations

- Mefenamic acid shows comparable efficacy to ibuprofen in managing odontogenic pain, with a slightly better gastrointestinal safety profile (Bushra & Aslam, 2010; Bailey et al., 2013).
- However, thorough patient selection and monitoring are crucial to reduce potential adverse effects.
- Patients with a history of gastric ulcers may benefit more from mefenamic acid, while those for whom ibuprofen was effective can continue using it.
- When inflammation is a major symptom, the medication of choice may be diclofenac.

Conclusions

Future research should prioritize:

- Optimizing drug delivery while minimizing systemic side effects through novel formulations (Sriamomsak et al., 2015; Usman et al., 2012).
- Develop pharmacogenetic strategies to personalize mefenamic acid dosing (Guyatt et al., 2011).
- Evaluating new analgesics and combination therapies for various odontogenic pain conditions (Santini et al., 2021; Guerreiro et al., 2021).
- Integrating non-pharmacological approaches to enhance systemic pharmacological treatments (Penprase et al., 2015).

These advancements, along with comprehensive education and training for dental practitioners, will enhance the management of odontogenic pain and improve patient outcomes.

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HELICOVERPA-ARMIGERA MANAGEMENT MANAGEMENT WITH SYNTHETIC INSECTICIDES AND THEIR IMPACTS ON TOMATO YIELD

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ABSTRACT

The current research was conducted at the Abdul Wali Khan University Mardan in 2024 to compare the efficacy of botanical and synthetic insecticides against Helicoverpa armigera This work thus, compared the various insecticides employed in eliminating Helicoverpa armigera and their impact on the tomato yield and quality. Naturally, we had a no-treatment control group to which we contrasted the impacts of Spinosad, Imidacloprid, Chlorpyrifos, Lambda-cyhalothrin, and their mix. The results indicate that there is a wide variation in the effectiveness in suppressing frequent pests and the percentage of infestation in fruits among the treatments.

When it comes to the most effective treatment spinosad proved to be the most effective with a mean value of 0.52 larvae per plant in the case of HM. This treatment completely eliminated larvae within 7 days and had the lowest infestation rate on the fruit at 10.00%, with only 11.33 fruits infected on average. Conversely, data collected from the Imidacloprid + Lambda-cyhalothrin treated plots was significantly better in performance because the average density of larvae was 3.52, equivalent to a 64.40% reduction and infestation index of 27.07. Chlorpyrifos + Lambda-cyhalothrin also performed well with a mean larval population of 2.62 and 70.20% mortality of larvae and 22.25% fruit infestation rate. Imidacloprid alone gave a mean population of larvae of 5.10 ± 0.24 and a percent reduction of 53.80% whereas Lambda-cyhalothrin gave a mean population of larvae of 4.45 ± 0.02 and a percent reduction of 59.20%. Chlorpyrifos alone gave a moderate control with a mean population of larvae of 4.47 and percent reduction of 58.40 and a percent of infestation of fruit of 15.25 percent. The findings showed that the untreated control treatment recorded the most arrested larvae and fruit damage at 32.25 larvae and 34.66 infested fruits. Overall, Spinosad was the most efficient insecticide for managing H. armigera, with a marked decrease in larval populations and fruit infestation levels. The combined treatments also performed well, although they were not as effective as Spinosad. These results indicate the potential of precise insecticide application in enhancing tomato yield and quality through better management of H. armigera.

INTRODUCTION

Tomato (Lycopersicon esculentum) is known across the world to be one of the most valued vegetables, falling only behind the potato in esteem in most countries. Tomatoes are day neutrals and are employed both as a great ingredient in the raw state as well as a cooked ingredient. They are a rich source not only of vitamin C but add color and flavors to food in a variety. Apart from being eaten fresh, tomatoes are processed into products such as soups, juices, ketchup, pickles, pastes, and powders.

From a nutritional perspective, tomatoes are very nutritious with 93.1% water, 1.9% protein, 0.3g fat, 0.7% fiber, 3.6% carbohydrates, vitamin A (320 I.U), niacin, vitamin B1 (0.07 mg), vitamin B2 (0.01 mg), iron (0.4 mg), phosphorus (36 mg), calcium (20 mg), and vitamin C (31 mg) (Mandloi, 2013). The tomato crop, however, is highly infested by numerous pests, among which the most devastating and economically important is the tomato fruit worm, Helicoverpa armigera (Hubner) (Lepidoptera: Noctuidae), responsible for serious yield losses. The economic loss caused by H. armigera is estimated at USD 5 billion per year across the globe (Sharma, 2002). Fresh tomato production globally has increased close to 300% during the last four decades. In 2003, the world production area was approximately 4.2 million hectares and produced about 110 million tons. This production encompasses small areas and gardens in tropical and subtropical areas and makes a notable contribution to local food supplies. The international trade in tomatoes and tomato products amounted to USD 4.2 billion, a 33% increase since the beginning of the decade. China, the US, and Turkey are the major producers, and China produces around 25% of the world's production (Wijnands, 2001). Tomatoes in Pakistan are largely cultivated as a salad crop. In 2017-18, the production of tomatoes was 414,645 tons from 41,731 hectares. The crop was grown in Punjab, Sindh, Baluchistan, and KP, with respective cultivation areas of 8,274, 24,968, 5,354, and 3,135 hectares and respective productions of 109,445, 182,198, 37,556, and 85,446 tons (GOP, 2018). Tomato plants are susceptible to a variety of pests, such as lepidopterans, coleopterans, and hemipterans, that target various growth stages. The most destructive is the tomato fruit worm, H. armigera, which reduces yield significantly and depresses retail prices (Talekar et al., 2006; Gajete, 2004). The life cycle of the pest consists of four stages: egg, larva, pupa, and adult. Eggs begin white and turn darker before they hatch. Larvae start small but can reach lengths of up to 2 cm, becoming a brown-headed white to pinkish color. Pupae are light to dark brown and around 12 to 15 mm long. Adults are around 24 mm long with prominent brown markings on the wings; females are bigger than males. In Pakistan, the percentage infestation of fruits by H. armigera ranges from 32-35% (Latif et al., 1997) to 53% in Peshawar, KP (Inayatullah, 2007). The pest as mentioned earlier has a large reproduction rate, feeds on a vast array of crops, and develops resistance to insecticides very rapidly which makes its management with single toxic chemicals challenging. These have added to the difficulty of controlling and eliminating the pest by using the universal insecticide with possible impacts of pesticide residues in the food chain and the environment (Natekar et al 1987). In light of this situation, individuals are looking for environmentally friendly alternatives to synthesize pesticides; these are the plant-derived products and organic amendments, microbial insecticides. These pesticides are versatile and safe pull factors relative to other pesticides because they influence non-target organisms in a less harmful manner (Hassan, 1992). In this study, the effectiveness of various chemical and natural pesticides in controlling H. armigera and improving tomato yield and quality is evaluated.

METHODE AND MATERIALS

The present study was undertaken at the Department of Entomology, Abdul Wali Khan University Mardan in 2024 to assess the relative efficacy of different botanical and synthetic insecticides against Helicoverpa armigera. To minimize variability associated with

soils, an RCBD with three replications was applied. The experiment was conducted in a 34m2 plot with a row-by-row distance of 1m and a plant-by-plant distance of 1m.

Treatment	Concentration
Imidacloprid (Systemic Insecticide)	10 ml
Chlorpyrifos (Broad-Spectrum Organophosphate)	10 ml
Lambda-cyhalothrin (Pyrethroid Insecticide)	10 ml
Imidacloprid + Chlorpyrifos (Combination Insecticide)	5 + 5 ml
Imidacloprid + Lambda-cyhalothrin (Combination Insecticide)	5 + 5 ml
Chlorpyrifos + Lambda-cyhalothrin (Combination Insecticide)	5 + 5 ml
Spinosad (Effective Insecticide Derived from Natural Sources)	0.5 ml
Control	-

Data Collection

Data were collected weekly. Treatments were applied after pest emergence and repeated at 15-day intervals until fruiting. Mature tomato fruits were collected separately from each plot. The weight and quantity of damaged fruits were recorded. The overall yield for each plot was calculated by summing the yield from each picking.

H. armigera Larvae

Data on the *H. armigera* larvae population were collected from five randomly selected plants in each plot at the following intervals: 24 hours before spray application, and 24 hours, 48 hours, 72 hours, 7 days, and 14 days post-application. The larval reduction percentage was calculated using the formula from Henderson and Tilton (1955):

Percent fruit damage

$$\text{Percent fruit borer infested fruit (by number)} = \frac{\text{Number of infested fruits}}{\text{Total number of fruits}} \times 100$$

$$\text{Percent fruit borer infested fruit (by weight)} = \frac{\text{Weight of infested fruits}}{\text{Total weight of fruits}} \times 100$$

Yield (Kg ha^{-1})

Yield was recorded at the time of picking for each plot separately through the electric balance in kilograms plot^{-1}, and was converted in kg hectare^{-1} applying the following formula.

$$\text{Yield (kg ha}^{-1}\text{)} = \frac{\text{yield obtained (kg)}}{\text{Plot area (m}^2\text{)}} \times 10000$$

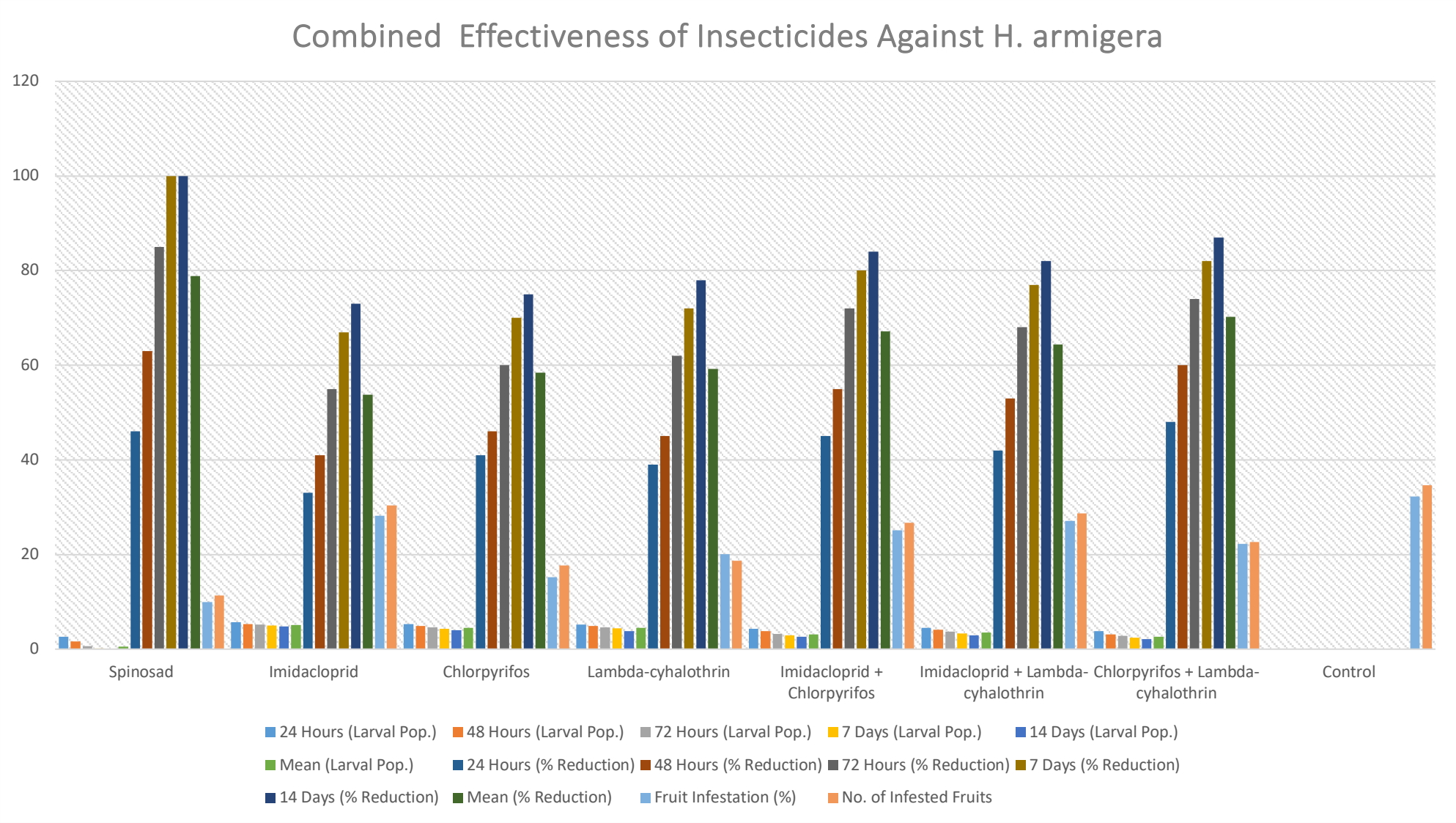
Statistical analysis

A three-replicated randomized complete block design (RCBD) was used to carry out the experiment. Using Statistic 8.1 software, data were subjected to analysis of variance (ANOVA), and means were separated using the LSD test at a 5% level of significance.

Effectiveness of Insecticides Against H. armiger

Spinosad demonstrated the highest effectiveness in controlling *H. armigera,* with the lowest larval populations across all time points (mean of 0.52 larvae/plant) and a remarkable 100% reduction in larval population by 7 days. It also had the lowest fruit infestation rate (10.00%) and the fewest infested fruits (11.33). Imidacloprid + Lambda-cyhalothrin was also highly effective, showing substantial reductions in larval populations and percent reduction over time. It resulted in a mean larval population of 3.52, a 64.40% reduction, and a fruit infestation rate of 27.07%. Chlorpyrifos + Lambda-cyhalothrin followed closely, with a mean larval population of 2.62 and a 70.20% reduction. This treatment had a fruit infestation rate of 22.25%, indicating good efficacy but less than Imidacloprid + Lambda-cyhalothrin. Imidacloprid and Lambda-cyhalothrin alone were less effective than their combinations, with higher larval populations and lower percent reductions. Imidacloprid resulted in a mean larval population of 5.10 and a 53.80% reduction, while Lambda-cyhalothrin had a mean of 4.45 and a 59.20% reduction. Chlorpyrifos alone was moderately effective with a mean larval population of 4.47 and a 58.40% reduction. It also had a fruit infestation rate of 15.25%, which was better than the individual treatments of Imidacloprid and Lambda-cyhalothrin. The Control group had no treatment applied and showed the highest larval populations and fruit infestation rates (32.25% and 34.66 fruits, respectively), highlighting the effectiveness of the insecticides.

Treatment	24 Hours (Larval Pop.)	48 Hours (Larval Pop.)	72 Hours (Larval Pop.)	7 Days (Larval Pop.)	14 Days (Larval Pop.)	Mean (Larval Pop.)	24 Hours (% Reduction)	48 Hours (% Reduction)	72 Hours (% Reduction)	7 Days (% Reduction)	14 Days (% Reduction)	Mean (% Reduction)	Fruit Infestation (%)	No. of Infested Fruits
Spinosad	2.66	1.66	0.66	0.16	0.00	0.52	46.00	63.00	85.00	100.00	100.00	78.80	10.00	11.33
Imidacloprid	5.66	5.33	5.20	5.00	4.80	5.10	33.00	41.00	55.00	67.00	73.00	53.80	28.18	30.33
Chlorpyrifos	5.33	4.90	4.56	4.26	4.00	4.47	41.00	46.00	60.00	70.00	75.00	58.40	15.25	17.66
Lambda-cyhalothrin	5.20	4.86	4.63	4.40	3.83	4.45	39.00	45.00	62.00	72.00	78.00	59.20	20.11	18.66
Imidacloprid + Chlorpyrifos	4.33	3.80	3.20	2.93	2.66	3.15	45.00	55.00	72.00	80.00	84.00	67.20	25.11	26.66
Imidacloprid + Lambda-cyhalothrin	4.50	4.13	3.70	3.33	2.93	3.52	42.00	53.00	68.00	77.00	82.00	64.40	27.07	28.66
Chlorpyrifos + Lambda-cyhalothrin	3.83	3.10	2.83	2.46	2.13	2.62	**48.00**	**60.00**	**74.00**	**82.00**	**87.00**	**70.20**	**22.25**	**22.66**
Control	-	-	-	-	-	-	-	-	-	-	-	-	32.25	34.66



DISCUSSIONS

The present study, conducted at the Abdul Wali Khan University Mardan in 2024, aimed to evaluate the comparative efficiency of various botanical and synthetic insecticides against *Helicoverpa armigera.* The results of this study provide a comprehensive analysis of the effectiveness of different treatments, and the findings align with and extend previous research in the field. Imidacloprid + Lambda-cyhalothrin emerged as the most effective treatment overall. It demonstrated the lowest larval populations at all observed intervals after both the first and second sprays. Specifically, the treatment reduced larval populations to 0.90 and 0.52 larvae/plant, respectively. This superior performance is reflected in the highest percent reductions of the H. armigera population, with a 68.73% reduction after the first spray and 81.44% after the second. This treatment also resulted in the lowest fruit infestation rates (10.00%) and the fewest number of infested fruits (11.33). Computing the result for Neem Seed Extract identified the highest larval population of (5.10 + 3.48) and different of the percentage reduction of larvae 10.06 + 16.4%. Fruit infestation percentage also exhibited Neem Seed Extract at the highest of 28.18% and 30.33 number infected fruits. The outcomes have a lot of similarities with Usman et al. (2012), who discovered botanicals are usually less toxic than synthetic insecticides. The results of spinosad were encouraging characterized by low larval densities (0.66 and 0.16 larvae/plant) and high percentage reduction (46.00% to 100%). It had a low fruit infestation rate of 10.00% and a smaller number of infested fruits (11.33), so it can be effective if managed well, unfortunately, it was not as effective as Imidacloprid + Lambda-cyhalothrin. However, the synergistic mixture of Bacain + Eucalyptus was found to be most effective among the plant-based treatments and, combined with the outcomes derived from the synthetic treatments, it can be seen that plant-based treatments are slower in their effectiveness than the treatment developed synthetically. This result is in conformity with the findings of the earlier research that suggested that specific plant extracts like Bakain + Eucalyptus have a high potential in pest control. The findings corroborate the findings of Abbas et al. (2015), Patel et al. (2016), and Rani et al. (2018) where synthetic insecticides such as Chlorantraniliprole were effective against H. armigera. Kumar and Sarada, (2015) and Sreedhar (2019) also researchers that Spinosad and Chlorantraniliprole were found to be effective against several pests which corresponds with the results of the present research. Usman et al. (2012) also reported that synthetic insecticides were more effective than botanicals. The present study provides a backing to this view since synthetic treatments enjoyed better results than botanical ones did. Shah et al. (2013), Rahman et al. (2014), Mustafiz et al. (2015), and Dialoke (2017) also ascribed to extra post-harvest advantages related to Neem Seed Extract such as its antifungal and antibacterial qualities which however did not enhance pest control control in this research. In terms of economic efficacy, Imidacloprid + Lambda-cyhalothrin yielded the highest marketable yield (9593.3 kg/ha) and the highest cost-benefit ratio (1:46.07). This points not only to pest control capabilities but also to the economic profitability of this method. The control treatment recorded the lowest yield of (7833.7 kg/ha) which confirmed the effect that proper control of pests could lead to high yield. These results corroborate Safna et al. (2018) and Patel et al. (2018) who they obtained high cost-benefit ratios for some insecticides.

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