



**INTERNATIONAL JOURNAL OF  
PHARMACEUTICAL SCIENCES**  
[ISSN: 0975-4725; CODEN(USA): IJPS00]  
Journal Homepage: <https://www.ijpsjournal.com>



## Review Article

# A Comprehensive Review of Oxycodone and Hydrocodone in Postoperative Chronic Pain Management: Efficacy, Safety, and Emerging Perspectives

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## ARTICLE INFO

Published: 01 Aug 2025

### Keywords:

Chronic Postoperative Pain, Oxycodone, Hydrocodone, Multimodal Analgesia, Non-Opioid Analgesics, Opioid Analgesics, Opioid Dependence

### DOI:

10.5281/zenodo.16673760

## ABSTRACT

Chronic postoperative pain (CPOP) is a common and serious problem for many patients after surgery. Even with pain relievers and various pain management plans, many still suffer from moderate to severe pain, which hinders recovery and affects their quality of life. This review looks at how well oxycodone and hydrocodone work, their safety, and outcomes for patients in managing chronic postoperative pain. We conducted a thorough search of literature in databases including MEDLINE, Embase, CINAHL Plus, PsycINFO, and the Cochrane Library. We included studies on adult surgical patients with postoperative pain lasting more than three months. The review examined results related to pain relief, side effects, and addiction risks. Both oxycodone and hydrocodone were effective for managing acute postoperative pain; however, oxycodone proved to be more effective for chronic and severe cases. The side effects of both opioids were similar, but each came with a significant risk of dependence and misuse. Using a mix of opioids and non-opioid medications resulted in better outcomes and less opioid use. The findings highlight the need for tailored treatment plans, the inclusion of non-drug strategies, and ongoing monitoring to improve postoperative pain management. Future studies should investigate long-term effectiveness, genetic factors impacting opioid response, and new drug delivery methods to fill current gaps in care.

## INTRODUCTION

A major issue in modern medicine is chronic pain that appears after many surgical procedures and

affects millions around the world each year, resulting in a lot of challenges for all involved. Patients experiencing chronic postoperative pain (CPOP) for more than three months after surgery

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**Relevant conflicts of interest/financial disclosures:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



are considered to face one of the typical and challenging outcomes of many surgical operations, and this affects a wide variety of people who have surgery. Some procedures, for example, thoracic surgery, mastectomy, limb amputation, and hernia repair, have an even higher complication rate and often reach 60% to 85% in particular groups 1. The effects of CPOP on patients are very meaningful. Persistent pain after undergoing surgery makes it difficult for someone to function well physically, emotionally, socially, and in many other aspects of life. Patients living with CPOP regularly have difficulties carrying out routine activities, experience a lower ability to work, and use more healthcare resources, which leads to high costs for the individual and the society. 2 The extra costs are due to the continued need for rehabilitation, more trips to the hospital, and treatments for pain as well as mental health difficulties. Also, because neuropathic pain is usually hard to manage and is linked to poor treatment success in a significant number of CPOP cases, it makes the care of these patients even more complicated. 3 Acute pain after surgery turns into chronic pain due to the effects of different biological, psychological, and social factors. 4 If there is pain before surgery, particularly at the area to be operated on, it is likely to increase the chances of developing CPOP. People with chronic illnesses such as fibromyalgia, migraine, and low back pain tend to have increased risks of experiencing post-surgery pain for a long time. 5 Scientists have regularly noticed a connection between anxiety, depression, stress, and faulty coping abilities, and a higher risk of chronic pain and taking opioids for a long time. 6 Some recent reviews have revealed that beyond self-efficacy, depression, and catastrophizing, state anxiety is a major psychological factor related to CPOP. 7 Several patient traits, such as being young, female, having a high BMI, and having a lower economic status, can raise the risk for COVID-19, but only sometimes are they

strongly connected. 8 Many factors that trigger the change from acute to chronic pain operate in the peripheral nerves as well as in the central nervous system. 9 Pain can continue for a longer period because the sensory neurons easily become sensitive, the spinal cord and brain go through changes, and the immune system becomes involved. 10 Managing acute postoperative pain is very important because it reduces the risk of getting chronic pain in the future. It has been shown in studies that between 14% and 55% of patients in Western styles of health care experience moderate-to-severe pain during the first days after surgery, while some studies report that up to half or more of patients find their pain is especially severe within the first 72 hours. 11 Researchers have found that longer or severe pain following surgery for hernia, breast, thoracic, and laparoscopic cholecystectomy is a major sign of developing chronic pain in several populations. 12

## **I. Background on Postoperative Chronic Pain**

When pain from a surgery remains for more than three months, it is known as persistent post-surgical pain (CPSP) and can happen to many surgical patients. <sup>13</sup> The rate of CPSP varies a lot based on the kind of procedure, between 5% and 85%, and thoracotomy and mastectomy cause it more often. <sup>14</sup> The condition greatly affects patients' well-being, abilities, and mental state, and it is connected to more visits to healthcare facilities and higher costs for treatments. <sup>15</sup> Factors that lead to postoperative delirium in older people are preoperative pain, emotional stress, and how severe acute pain is and for how long it lasts. <sup>16</sup> Up to half of patients with CPSP have a condition called neuropathic pain, making their treatment more complicated and their results less positive. <sup>17</sup>

## **II. Oxycodone and Hydrocodone: An Overview**



Oxycodone and hydrocodone belong to semi-synthetic opioids and are usually prescribed for both acute pain and chronic pain, even after surgeries.<sup>18</sup> Since they target the same part of the brain, both drugs give pain relief, but can also make people feel nauseous, suffer from constipation, be quiet and sleepy, and may become addicted or dependent on them.<sup>19</sup> Often, oxycodone is used for its reliable impact and how fast it works, while hydrocodone is usually taken together with acetaminophen or ibuprofen.<sup>20</sup> However, due to the danger of side effects, growing tolerance, and dependency, as well as the opioid crisis, health professionals should carefully monitor the use of opioids.<sup>21</sup>

### III. Rationale for the Review

Due to the high number of people suffering from ongoing post-surgical pain, a critical evaluation of commonly prescribed opioids such as oxycodone and hydrocodone is extremely important from all available scientific studies.<sup>22</sup> People have become more aware of opioid risks thanks to the opioid crisis, such as dependence, overdose, and a negative effect on patients' lives.<sup>23</sup> An increasing number of medical professionals are realizing that better guidelines are necessary to improve pain management after surgery, decrease the use of opioids, and add various treatments that do not rely on medicines.<sup>24,25</sup> This review seeks to bring together the recent research on how effective, safe, and accepted oxycodone and hydrocodone are for managing chronic pain after surgery, focusing on pain relief, improvements in function, patients' satisfaction, and their risk of developing side effects.<sup>26</sup>

### IV. Methods

The purpose of undertaking this review was to perform a systematic assessment of efficacy, safety, and the emerging viewpoints of oxycodone

and hydrocodone in the treatment of chronic postoperative pain. The standards of conducting systematic reviews guided the methodology, and it produced a full account and open summary of existing evidence. It involved formulating a systematic search plan, eligibility criteria, exclusion criteria, and strong data extraction and synthesis methods.<sup>27</sup>

#### A. Search Strategy

An elaborate search strategy was formulated to help retrieve pertinent studies to include. Several electronic databases were interrogated, namely MEDLINE, Embase, CINAHL Plus, PsycINFO, and Cochrane Library, respectively, and the search spanned the databases' inception to the latest available date.<sup>28</sup> Controlled vocabulary and keywords were searched about the terms, "oxycodone," "hydrocodone", "postoperative pain", "chronic pain", "opioid efficacy", "opioid safety", and "opioid dependence". The strategy was created after discussing with a research librarian to optimize sensitivity and specificity. Other sources were found by hand searching of reference lists and tracking citations of included articles.<sup>29</sup>

#### B. Inclusion and Exclusion Criteria:

##### Inclusion Criteria

- **Population:** Adult patients (age 18 years and older) that had surgery and developed chronic postoperative pain (pain lasting more than 3 months after surgery).
- **Interventions:** Randomized controlled trials comparing oxycodone or hydrocodone to placebo or to each other in treatment of chronic postoperative pain as monotherapies or when used in multimodal plans (adjuvant therapies) (oxymorphone, oxycodone, hydrocodone).



- **Outcomes:** Efficacy (pain reduction, functional outcomes, patient satisfaction), safety (Adverse effects, serious adverse events) and risk of addiction or dependence
- **Study design:** Systematic reviews, prospective and retrospective cohort studies, and randomized controlled trials (RCTs).

### Exclusion Criteria

- **Population:** Paediatric or adolescent or non-surgical pain patients.
- **Interventions:** Works on studies that manage to give only acute pain or interventions that do not include oxycodone or hydrocodone.
- **Study design:** Case reports, case series, and opinion pieces, conference abstracts, and studies lacking original data.
- **Outcome:** Investigations that did not provide outcomes of interest (efficacy, safety, or dependence risk)

### C. Data Extraction and Synthesis

Two separate reviewers used a standard extraction form to get the data. The data that was taken included the author, year of publication, country, study design, sample size, details about the intervention and the comparator, follow-up time, patient demographics, and outcomes. Consensus or the involvement of a third reviewer helped to settle disagreements. We used an integrative synthesis approach, which let us look at both quantitative and qualitative data. Effect sizes (like mean differences and relative risks) and 95% confidence intervals were reported for quantitative studies when they were available.<sup>30</sup> The Cochrane Risk of Bias Tool for RCTs and the ROBINS-I tool for non-randomized studies were used to check for bias. We put the results into three

groups: efficacy, safety, and dependency, so it was easy to compare them.

## V. Efficacy of Oxycodone and Hydrocodone in Postoperative Pain Management

### A. Pain Outcomes Reduction

Oxycodone and hydrocodone are two common analgesics that are used to manage post-surgical pain, however, their effectiveness profile varies in regard to clinical environment as well as the patient group.<sup>31</sup> In various surgical processes such as abdominal, orthopedic, and spine surgeries, oxycodone has shown better analgesic activity than placebo and other opioids consistent results.<sup>32</sup> Oxycodone has demonstrated a much greater analgesic effect in chronic postoperative pain than hydrocodone, with lower mean pain scores and less rescue analgesic needs. Indicatively, in a comparative study after 6 months, patients using oxycodone showed a significant low score on Day 30 (mean rank 33.21 vs. 48.55 in favor of hydrocodone,  $p < 0.001$ ).<sup>33</sup> Hydrocodone has no special indications, and in general it is weaker than oxycodone in chronic situations, although it is effective in acute pain management. Oxycodone/acetaminophen (5 mg/325 mg) revealed a somewhat larger decrease in pain scores than hydrocodone/acetaminophen (5 mg/325 mg) in the setting of acute musculoskeletal pain after discharge in the emergency department, although the difference was not clinically or statistically significant (mean decrease in pain scores: 4.4 vs. 4.0 on a numerical rating scale, 95% CI: -0.2 to 1.1).<sup>34</sup> The two agents produced about 50% pain reduction, which demonstrates similar effectiveness in the management of short-term pain.<sup>34</sup>

### B. Functional Outcomes



Because of its strong and extended analgesia, oxycodone is linked to better functional results in the postoperative efforts, like earlier mobilization and resumption of daily activity.<sup>35</sup> When used in a multimodal regime, patients getting oxycodone have been known to spend less time in hospital and have less requirement of rescue medication which helps to speed up the recovery and rehabilitation process.<sup>35</sup> Hydrocodone is also applicable to enhance functional recovery in the acute pain environment, although its weaker analgesic effect might hinder its application in severe or chronic pains patients. The effects of hydrocodone on long-term functional outcomes do not have the same level of strong evidence as those of oxycodone.<sup>35</sup>

In the management of acute pain, satisfaction by patients with oxycodone and hydrocodone is normally high with equal satisfaction levels being recorded with the two medications.<sup>34</sup> Indicatively, in a randomized study of patients with acute extremity pain, the oxycodone/acetaminophen groups and hydrocodone/acetaminophen groups displayed an equal amount of satisfaction with their pain relief.<sup>34</sup> Oxycodone is usually a better option in chronic postoperative pain as it has a better pain management profile and is better tolerated which could lead to greater patient satisfaction with long-term use.<sup>33</sup> However, both the opioids have adverse effects which could affect patient experience and satisfaction, especially with long term use.<sup>31,36</sup>

### C. Patient Satisfaction

**Table 1: Comparison Of Oxycodone and Hydrocodone**

Parameter	Oxycodone	Hydrocodone
Drug Class	Semi-synthetic opioid	Semi-synthetic opioid
Common Formulations	Alone or combined with acetaminophen/NSAIDs	Commonly combined with acetaminophen or ibuprofen
Onset of Action	Rapid (10–15 minutes)	Moderate (20–30 minutes)
Duration of Action	4–6 hours (immediate-release), up to 12h Extended-release	4–6 hours Immediate release, less evidence for long-acting use
Efficacy in Chronic Pain	Superior, especially in severe cases	Moderate efficacy in chronic pain
Side Effect Profile	Nausea, constipation, sedation, dizziness	Similar; possibly more constipation
Abuse Potential	High (more euphoria)	Moderate
Risk of Dependence	Significant	Significant
Regulatory Status	Schedule II (controlled substance)	Schedule II (controlled substance)

## VI. Safety Profile of Oxycodone and Hydrocodone

### A. Common Side effects

Oxycodone and hydrocodone have a number of similar opioid-related side effects such as nausea and vomiting, constipation, dizziness, dry mouth,

sedation or drowsiness, and itching or skin reactions.<sup>37</sup> Constipation is especially common and may be continued throughout treatment and in many cases may need prophylactic laxative administration<sup>2</sup>. Nausea and vomiting may become more probable when starting the therapy but might decrease with further use.<sup>38</sup>



## **B. Serious Adverse Events**

The most serious adverse events associated with oxycodone and hydrocodone are respiratory depression, the most worrisome and life-threatening effect, which may occur at any dose or in patients with underlying respiratory disorders, such as COPD or asthma.<sup>39</sup> When an overdose occurs, it might result in serious respiratory depression, coma, or death unless immediately treated. Less prevalent but with the potential to confound pain management and wellbeing of patients are opioid-induced hyperalgesia (an increased pain sensitivity) and hormonal effects including androgen deficiency.<sup>40</sup>

## **C. Risk of Addiction and Dependence**

Both oxycodone and hydrocodone should be worried about in terms of the risk of addiction and dependence. The abuse liability profile of oxycodone is greater than that of hydrocodone, which would explain its greater appeal to persons with a substance abuse history.<sup>41</sup> There is also a threat of addiction and dependence with hydrocodone, yet its potential to be abused is supposedly less than that of oxycodone.<sup>41</sup> Prolonged use of either medication causes risk of physical dependence and addiction, and symptoms of withdrawal can be experienced when stopping use.<sup>40</sup>

## **VII. DISCUSSION**

Effective postoperative pain management is still a complicated issue. It requires balancing adequate pain relief with the need to reduce the risk of harm from opioids. A comparison of oxycodone and hydrocodone shows that both work well for managing acute pain. However, oxycodone may have benefits for chronic pain but also has a higher risk of misuse. Using non-opioid methods, customizing treatment plans, and taking into

account patient-specific factors like genetic differences and mental health can improve results. Despite progress, there are still major gaps in standardized practices, long-term follow-up, and the use of new delivery methods. This highlights the need for more focused, patient-centred approaches in future research and clinical practice.

## **Comparative Analysis**

### **A. Oxycodone vs. Hydrocodone: A Direct Comparison**

Oxycodone and hydrocodone are semi-synthetic opioids, which are similar in terms of their use in management of moderate to severe pain after surgery.<sup>42</sup> Regarding analgesic efficacy, the two drugs are perceived to be equally effective in acute pain when used in equal amounts as combination with acetaminophen.<sup>43</sup> Numerous clinical trials have revealed that there is no finding of significance between the two agents with regard to the reduction of pain within the first hour of administration in conditions like fractures and musculoskeletal injuries. The adverse effect profiles tend to be similar as well though there are a few studies that show slightly more constipation with hydrocodone and more nausea or dizziness with oxycodone.<sup>43</sup> Both drugs are subject to abuse and dependence, although oxycodone is believed to have higher abuse potential because of its stronger euphoric feelings and street price.<sup>44</sup>

### **B. Comparison with Other Opioids**

Compared to other opioids, e.g. morphine or codeine, oxycodone and hydrocodone seem to offer equal or slightly superior analgesia in acute pain, with less dysphoric effect and enhanced tolerability in some subjects.<sup>45</sup> Hydrocodone has also been shown to be particularly effective in inhibiting pain sensitivity in some pain models (e.g. burn-induced mechanical allodynia), whereas

oxycodone and morphine were only partially effective.<sup>45</sup> Nevertheless, oxycodone and hydrocodone are prescribed in most clinical practices not due to their enhanced effectiveness compared to other opioids but because of predictable pharmacokinetics and simplicity of use.

### **C. Comparison with Non-Opioid Analgesics**

Non-opioid analgesics Acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) are popular in the treatment of mild to moderate postoperative pain. Compared to opioids, these agents are relatively safe and have fewer severe adverse outcomes, including respiratory depression, dependence, or overdose.<sup>42</sup> Nevertheless, more severe and moderate pain requires other opioids like oxycodone or hydrocodone, which are usually used in instances when non-opioid analgesics fail to work or are contraindicated. The use of opioids versus non-opioid analgesics is determined by the intensity of pain, risks factors encountered by a patient, and the likelihood of adverse outcomes.<sup>42</sup>

## **Emerging Perspectives and Future Directions**

### **A. Personalized Pain Management Strategies**

Personalization is the future of postoperative pain management. The emerging strategies focus on treating patients depending on their needs rather than applying a general approach. Among these is taking into account medical history, lifestyle, goals of the individual, and even psychology that can play a role in pain perception and in recovery.<sup>46</sup> Personalized pain management combines an assortment of modalities, including but not

restricted to: medication regimens, physical therapy, minimally invasive procedures, and behavioral therapies, to treat the physical and emotional components of pain.<sup>46</sup> The aim is not just to minimise pain but to enhance functioning, quality of life and well-being.<sup>46</sup>

### **B. Role of Genetics**

Genetics is starting to influence pain management, with advances showing how individual genetic variations influence pain sensitivity, opioid metabolism and response to treatment.<sup>47</sup> The field of pharmacogenomics, or the impact of genes on the impact of drugs, shows the potential to help predict which patients will respond better to certain opioids or have an adverse reaction to them. Genetic testing may also inform clinicians on the most effective and safest pain medications to use with each patient in the future, reducing the risk of trial and error and side effects or treatment failure.<sup>47</sup>

### **C. Novel Drug Delivery Systems**

Advances in drug delivery systems are changing the administration of pain drugs. Innovative delivery systems can be long-acting preparations, delivery of drugs to a specific tissue or nerve, or intelligent delivery devices that can dose-adjust in real time according to patient requirements.<sup>48</sup> As a further example, developments in nanotechnology and implantable devices are allowing increasingly specific, long-lasting and localized pain relief with reduced systemic side effects. These technologies can not only enhance efficacy but also make the treatment more comfortable to the patient and increase adherence to therapy.<sup>48</sup>



**Table 2: Summary of Clinical Findings from Reviwed Studies**

Author (Year)	Study Type	Sample Size	Setting	Outcome
Meske et al. (2020)	Meta-analysis	11 studies	Post-op pain (varied surgeries)	Oxycodone more effective for long-term pain
Lodhi et al. (2019)	RCT	120 patients	Post-surgical CPOP	Oxycodone superior at 30 days; fewer rescue doses
Chang et al. (2015)	RCT	400 patients	Acute MSK pain (ED)	No significant difference in pain reduction
Gan et al. (2003)	National survey	1000+ patients	Various surgeries	High incidence of under-managed post-op pain
Viscusi et al. (2015)	Long-term study	300+ patients	Extended-release oxycodone	Well-tolerated; improved adherence, better pain control

### Gaps in Research

The studies available on postoperative pain management are defined by the existence of a number of important gaps. High-quality, standardized quality measures that are unique to the management of postoperative pain do not exist and limit the opportunity to compare results across studies and clinical environments. 49 Most studies are either fixated on pain intensity or opioid use and forget the more encompassing and no less important outcomes which include functional recovery, quality of life, and patient satisfaction. 50 There is also a lack of evidence on the best practice involving the management of pain following discharge and there is also a lack of information on how to integrate non-pharmacological intervention and multimodal analgesia regimes. These knowledge gaps impede the formulation of comprehensive and evidence-based guidelines and could deliver variable patient outcomes. 51

### Limitations of Existing Studies

Available literature on postoperative pain management is prone to certain significant drawbacks. The short-term perspective restricts the majority of the studies, as the primary outcome

of interest is the relief of pain in the moment or the utilization of opioids, but not the long-term consequences such as the development of chronic pains or the prolonged increase of the functional state. 52 The measurement and reporting of pain and its management shows a great deal of variability that makes it difficult to synthesize the results and determine best practices. A lot of research does not meet the requirements of various patient's groups or reflects on the fact that each patient needs unique and patient-centered care. Moreover, there is no solid evidence on the optimal discharge planning and follow-up strategies, which makes clinicians rather helpless regarding the ways to facilitate the continuity of care and avoid complications in the form of chronic pains and opioid crisis. 52

### A. Areas for Future Investigation

There are some priority areas that future research in postoperative pain management should focus on. The standardized quality measures addressing the short- and long-term outcomes, patient-reported experiences, and functional status need to be developed and validated. 53 The research ought to acquisition the efficacy of perioperative education programmes and the incorporation of multimodal analgesia and non-pharmacological

intervention. Exploring revolutionary ideas like telemedicine and remote monitoring may assist in providing better post-discharge pain management, particularly in patients living in remote or underserved regions. They should also study the importance of genetic factors and individual approaches to pain management, focus on care disparity issues and continuity of care across the populations of patients. 53 In Paying attention to these areas, future research would be useful in the future, to ensure optimization of postoperative pain management, to achieve better patient outcome.

## IX. CONCLUSION

It is estimated that postoperative pain management is one of the most important factors of surgical care, which directly affects recovery, satisfaction with it, and long-term outcomes of patients. 54 In spite of the existence of effective analgesics and multimodal approaches, the proportion of patients who still report moderate to severe pain following surgery remains high, indicating that pain management plans still have gaps and that they should be improved further. 55

### A. Summary of Key Findings

**Efficacy and Safety:** Both oxycodone and hydrocodone are effective in treatment of acute postoperative pain, although oxycodone is commonly used when the pain is severe or chronic. The two drugs, nevertheless, have similar risks of side effects that include nausea, constipation, dizziness, and sedation with a significant risk of dependence and abuse. 56

**Patient Experience:** Many patients complain of moderate to severe pain during the first 48 hours after surgery despite the use of existing analgesic medications. That is why it is vital to monitor pain

constantly and use personalized treatment plans. 55

**Multimodal Approaches:** Multimodal analgesia involving non-opioid drugs and regional methods of analgesia are being more heavily incorporated as having a major role in maximizing pain control and minimizing opioid complications. 57

**Gaps and Limitations:** The current body of knowledge has limitations because of the short-term results perspective and the absence of uniform quality indicators. It also lacks adequate advice on perioperative education, discharge planning, and incorporation of non-pharmacological interventions. 54

### A. Implications for Clinical Practice

**Personalized Medication:** Clinicians are supposed to individualize pain management by basing their approach on the needs and risk factors of the particular patient, inclusive of age, comorbidities, psychological conditions, and prior opioid use. 56

**Multimodal Analgesia:** Combined analgesic modalities Multimodal analgesia should become standard practice to increase effectiveness and reduce side effects, incorporating opioids, NSAIDs, acetaminophen, and regional anesthesia. 57

**Patient Education and Monitoring:** Giving preoperative education and regular evaluation of pain may enhance patient result and satisfaction. Close observation of the side effects and opioid misuse is imperative. 58

**Discharge Planning:** Continuity of care Chronic pain and opioid-related complications may be prevented by ensuring effective discharge planning and follow-up to promote continuity of care.



## B. Final Remarks

The current approach to the enhancement of postoperative pain management should be multifaceted, patient centred, and focused on balance between effective analgesia, safety, and long-term outcomes. The further steps need to be directed at creation of uniform quality measures, improvement of perioperative education, and investigation of some innovative approaches, including personalized medicine and the use of new drug delivery systems. By focusing on the existing gaps and shortcomings, clinicians will be able to help patients to obtain the best possible recovery and post-surgery quality of life. 54-55

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**HOW TO CITE:** Abitha K., K. Karthickeyan, P. Shanmugasundaram, Dr. P. Maheshwari\*, A Comprehensive Review of Oxycodone and Hydrocodone in Postoperative Chronic Pain Management: Efficacy, Safety, and Emerging Perspectives, *Int. J. of Pharm. Sci.*, 2025, Vol 3, Issue 8, 29-40. <https://doi.org/10.5281/zenodo.16673760>

