

# The Emerging Role of Dexmedetomidine hydrochloride in Dissolving-Microneedle Technology and Therapeutic Applications

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## Abstract

Dexmedetomidine hydrochloride (DEX) is an effective sedative that is often used in intensive care units due to its minimal impact on the respiratory system. Although DEX has shown encouraging analgesic benefits, its traditional intravenous administration entails slow infusion, increasing the risk of infection and jeopardising patient compliance and comfort. DEX microneedle products use tiny-sized needles, so compared with injections using regular-sized needles, the patient's discomfort will be reduced. Dissolving microneedles achieve intradermal drug administration and penetrate the stratum corneum barrier, which greatly increases medication bioavailability as compared to traditional transdermal drug delivery methods. However, barriers such as high treatment costs and patient concerns about side effects may hinder its market growth. At present, there are a few research studies on the experience of using DEX microneedle products. The purpose of this review is to provide context to enhance comprehension of the properties and uses of the new alpha2-adrenoceptor agonist DEX in dissolving-microneedle technology and therapeutic applications. Further research may explore expanded indications for this formulation.

**Key words:** Dexmedetomidine hydrochloride, dissolving-microneedle technology, medicine, therapeutic applications

## Introduction

Dexmedetomidine (DEX) is a highly selective  $\alpha_2$ -agonist having sedative, analgesic, and sympatholytic effects [1, 2]. DEX appears to be the perfect sedative due to its little effects on the respiratory system. It has not been utilized extensively due to its restricted indications for treating patients who are intubated, mechanically ventilated, and admitted to an intensive care unit [3]. DEX reduces the chance of respiratory depression and produces a modest kind of drowsiness. Main uses for this medication include: (1) mild sedation in critical care, however long-term sedation is not advised; and (2) anaesthesia, either as a stand-alone sedative or as a co-adjuvant to general anaesthesia. DEX has demonstrated intriguing respiratory, anti-inflammatory, cardiovascular, and organ protecting qualities in both situations. Its analgesic and anxiolytic properties are employed in the clinic for surgical sedation and critical care [4].

The biological activities of DEX have been shown through a variety of signalling pathways in several animal models. DEX has been administered by a variety of methods with varying bioavailability, despite its development for intravenous usage. Patients have employed intramuscular, nasal, or buccal (submucosal) delivery as well as microneedling administration with effectiveness [5, 6].

DEX can be used for general anaesthesia, local anaesthesia, spinal anaesthesia and nerve-blocking anaesthesia in clinical procedures [7]. It provides good sedative and analgesic effects during surgery and does not induce respiratory depression [8]. DEX, which can shield the nerves, also reduces the amount of time it takes for patients to regain consciousness following procedures. Brainstem tumour surgery is among the most challenging and risky surgical procedures because of the brainstem's tiny size, high number of nerves, and widespread distribution. Accidents frequently occur during this type of surgery [9].

DEX, the pharmacologically active dextroisomer of medetomidine, is an imidazole compound with specific and selective  $\alpha_2$ -adrenoceptor agonism. The mode of action is distinct and not like those of sedatives that are already in use, such as clonidine. Receptors in the brain and spinal cord are activated to inhibit neuronal activity, which causes bradycardia, hypotension, sedation, and analgesia. Other responses to receptor activation include decreased gastrointestinal tract salivation, secretion, and motility; contraction of smooth muscle, including vascular and other; inhibition of renin release, increased glomerular filtration, and increased sodium and water secretion in the kidney; decreased intraocular pressure; and decreased pancreatic release of insulin [10]. A distinctive characteristic not seen with other therapeutically accessible sedatives was that most patients receiving DEX as a main treatment had clinically effective drowsiness but were nevertheless easily arousable [11].

DEX can be an alternative long-term sedative for accomplishing sedation objectives. The main benefit of DEX is that it lowers the risk of delirium and coma when used for extended periods of time in an intensive care unit. It is certain that there may be side effects like bradycardia while using DEX for brief periods of time. It's interesting to note that using DEX also lowers the risk of infection; this seems to be because using DEX shortens the time a patient must stay in an intensive care unit and/or requires mechanical ventilation. At the conclusion of extended sedation, rebound and/or withdrawal symptoms do not appear to be a problem [12].

According to WHO estimates, 30% of nations worldwide lack medication control and rules. Pharmaceutical product quality may be improved primarily by strengthening drug and health regulatory agencies, creating reasonably priced medicinal formulations, and increasing product quality. On the other hand, data with a suitable sample size and a random sampling methodology are critically needed for both the critical assessment of the prevalence of medications of low quality [13]. These kinds of data are necessary in order to assess their efficacy, implement suitable treatments, and monitor changes over time. These include the ability not only to assess the immediate effects of the microneedling therapy but also to measure the bioactivity of the added drug, as well as providing insight into the long-lasting effects and morphology changes of the skin [14].

#### **DEX: An Innovative Sedative Agent**

DEX is an innovative sedative agent in the medical field, especially in the field of dermatology [15, 16]. DEX belongs to a class of medication called alpha-2 receptor agonists. Its primary role is for the sedation of adult patients in an intensive care unit [17, 18]. It may be utilized in the microneedling setting as an off-label topical sedative. However, researchers have found that there are several advantages of using DEX over the traditional sedatives like lidocaine or 2% lignocaine with adrenaline. First of all, patients do

not suffer from allergic side effects. Secondly, it has a longer duration of action. Thirdly, there's a quicker onset of action, leading to rapid and more effective skin anesthesia. Lastly, the depth of the skin to be punctured can be easily adjusted due to the biphasic dose response of DEX, which may promote a better procedural efficacy [19, 20]. However, this will definitely unveil challenges for the current market of microneedling products and need the practitioners to acquire the knowledge of handling this new product. Because the unique formula of DEX promises a better option for patients with needle phobia and dermatologists might develop a preference to choose DEX over lidocaine.

In addition, because the health benefits of microneedling in stimulating collagen formation, promoting wound healing and reducing wrinkles and acne scars have received more research support either in the laboratory or in clinic, the minimal invasive nature of microneedling promotes a trend of home based therapy under the instruction of a general practitioner. This will substantially boost the consume of DEX. However, under the idea of 'Innovation Cycle', cost may be a main prohibitory factor for patients to receive the therapy. Greater cost of a more effective and less painful product might hinder the initial uptake of DEX on the market at least for the first few years after it's introduced. Finally, the ethical and lawful administration of an off-label medication should never be overlooked. Its practitioners' responsibility to stay current and well informed on such controversy. Eminently, practicing under The Off-Label Use of Drugs should be exercised; but in the event of best practice, consent of the patient should have obtained after the provision of full information [21-25].

#### **Clinical Research on DEX**

DEX is a highly selective  $\alpha_2$  adrenergic receptor agonist that has several useful features. These include opioid analgesic and anesthetic-sparing action, central sympatholytic impact, arousable sedation that resembles natural sleep, and cardiovascular stabilizing ability. There is no respiratory depression and only a little hemodynamic impact as a result of DEX's dose-dependent sedation of the locus coeruleus [26, 27]. It is used in perioperative medicine for several off-label reasons, including procedural sedation, for which it is licenced. Additionally, the European Medicines Agency has licenced it for analgesia and sedative since 2017 [28]. DEX possesses several admirable properties including its ability to effectively reduce delirium without impairing breathing. Nevertheless, because of its peripheral vasoconstrictive and sympatholytic actions, it might cause momentary hypertension, bradycardia, and hypotension [29].

The DEX area has several hot spots, including pharmacokinetics and pharmacodynamics, sedation and outcome in intensive care units, pain treatment and nerve block, and premedication and usage in children. These findings were shown using co-cited reference analysis and keyword analysis. Future study should focus on the effects of DEX's analgesic action, organ-protective qualities, and sedation on the outcomes of critically sick patients [30].

Patients who have suffered a stroke are frequently older and suffer from comorbid conditions that increase their risk of surgical complications under anaesthesia, such as respiratory depression. In this study, the therapeutic effects of etomidate fat emulsion and DEX mixed under anaesthesia were investigated in patients receiving interventional stroke therapy. In patients having interventional stroke therapy while under anaesthesia, DEX in combination with etomidate fat emulsion has the potential to be

useful in clinical settings by maintaining optimal hemodynamics and lowering complications [31].

The present study outlines the modes of administration, pharmacological effects, and application categories of DEX. The clinical use of DEX is encouraging, but it is still in its infancy, and further study is needed to fully comprehend its pharmacological characteristics, patient selection, dose, and side effects [32].

### **DEX Uses**

The FDA-approved uses for DEX include peri-procedural (or peri-operative) sedation of non-intubated patients and sedation of intubated and mechanically ventilated patients in the intensive care unit (ICU). Off-label uses have been introduced over time, including supplemental analgesia, ICU insomnia therapy, alcohol withdrawal treatment, and delirium prevention and treatment. Because it frequently induces a sedative state that makes patients comfortable and cooperative during mechanical breathing, its indications have been broadened. Furthermore, as it does not significantly lower breathing, it is safe to use on patients who are not intubated and does not require interruption to achieve extubation. Since most sedatives lack intrinsic analgesic qualities, DEX has an opioid-sparing effect [33]. It has been shown that, in comparison to other sedatives, ICU sedation with DEX can reduce the incidence, duration, and postpone the development of delirium [34]. When treating elderly patients who have had heart surgery, this effect has proven to be quite helpful [35].

DEX is frequently utilised in anaesthesia practices. It is employed in a number of procedures for procedural sedation. Additionally, it is commonly used to sedate patients during awake intubation procedures. For the above mentioned reasons, it is perfectly appropriate for this indication. Another adjunct infusion used during general anaesthesia is DEX. There is proof that DEX reduces nausea, postoperative pain, and the need for opioids [36]. The use of DEX as an adjuvant to avoid surgical delirium, emerging agitation, and cognitive impairment has generated some attention. Research supports the idea that emerging agitation may be prevented in both adults and children [37]. DEX has also been used in peripheral nerve blocks to extend the duration of analgesia [38].

DEX produces a level of deep sedation in which patients are able to participate with nursing care, open their eyes to verbal stimulation, and accept basic orders. It possesses sedative and analgesic qualities without respiratory depressive effects. With these degrees of sedation, it is therefore a highly helpful medication for patients who can be kept on mechanical ventilation without experiencing the negative consequences of over- or infrasedation. Comparing the usage of DEX to other sedatives, a decreased frequency of delirium has been linked to the former. It may also be helpful in sedating individuals receiving non-invasive ventilation [39].

### **Mechanism of Action of DEX**

DEX, an alpha agonist, possesses sedative, anxiolytic, hypnotic, analgesic, and sympatholytic properties. It works by blocking the brainstem's alpha receptors, which prevents norepinephrine from being released, so suppressing central sympathetic outflow. Compared to alpha1, it has a 1600 to 1 selectivity for the alpha2 receptor. Comparing this selectivity to clonidine, another alpha agonist with a selectivity of 220 to 1, is particularly noteworthy. While the exact method by which DEX may lengthen the duration of a peripheral nerve block is unknown, it is thought that, rather

than a systemic or central mechanism, it is more likely a perineural mechanism that works by obstructing the cation current [40].

### **DEX in Intensive Care**

DEX is a medication commonly used in intensive care settings for sedation of mechanically ventilated patients. Clinical research indicates that DEX is appropriate for both short- and long-term sedation in an intensive care unit. It is also linked to a shorter duration of mechanical ventilation, a quicker time to extubation, and patients who are more cooperative, easier to rouse, and have better communication skills than those on midazolam or propofol [41]. Further randomised controlled trials show that patients treated with DEX had more days free from delirium and coma than patients treated with lorazepam. They also have a lower incidence of delirium when compared to patients treated with propofol, midazolam, or remifentanyl [42]. In summary, DEX is a valuable sedative agent in the intensive care setting due to its unique pharmacological properties, including minimal respiratory depression, hemodynamic stability, and preservation of patient cooperation. However, its use should be carefully monitored for potential adverse effects, and appropriate dose titration is essential to achieve optimal sedation while minimizing complications.

### **DEX as Neuroprotective Agent**

DEX has gained attention for its potential neuroprotective properties, particularly in the context of various neurological disorders such as ischemic stroke, traumatic brain injury (TBI), and neurosurgery. While the exact mechanisms underlying its neuroprotective effects are not fully understood, several studies have suggested potential mechanisms and provided evidence supporting its use as a neuroprotective agent. Research on the role of DEX in neonatology and anaesthesia has been particularly interesting since the drug's many benefits were reported, including improved post-operative recovery, decreased opioid prescriptions, decreased sympathetic tone, inhibition of inflammatory reactions, and organ protection. Research on the mechanism of action has connected the neuroprotective effects of DEX to its dependent or independent control of neuroinflammation, apoptosis, oxidative stress, and synaptic plasticity via the  $\alpha_2$ -adrenergic receptor [43]. The role of DEX as a neuroprotectant agent has been confined to animal experimental models. The aetiology of neural injury is a multifaceted process that encompasses several molecular pathways. Different forms of neuronal damage, including as necrosis, apoptosis, oxidative stress, and so on, are treated with a variety of neuroprotective drugs. Inflammatory indicators and molecular pathways are modulated by DEX, demonstrating its neuroprotective potential [44].

Numerous mechanisms, including signal transmission, hormone and peptide release, and cell damage, result in the release of neurotransmitters. Prior research has shown that nerve injury causes the release of excitatory neurotransmitters from the nerve terminal, such as glutamate and aspartate. Additionally, these excitatory neurotransmitters cause more nerve injury [45]. Programmed cell death, or apoptosis, frequently happens in the aftermath of an injury and is essential to proper growth of tissues or organs [46]. The immunological or inflammatory response's significance is not fully understood since, while it increases oxidative stress, its phagocytes also aid in maintaining neurogenesis and can kill or injure nerve cells. A multitude of chemicals, including pro-inflammatory cytokines (TNF, interleukins), chemokines, and inflammatory cells (lymphocytes,

macrophages, natural killer cells (NKC), astrocytes, and monocytes) are involved in the intricate process of inflammation, also known as neuroinflammation [43].

Anesthesia-induced neurotoxicity is a group of detrimental side effects linked to the administration of anaesthesia that affect the central or peripheral nervous systems. Certain research indicates that early anaesthesia exposure may have long-term behavioural impacts on people. DEX functions as a sedative and analgesic by modulating cellular processes and affecting intracellular signalling through its agonist actions on imidazoline type 2 (I2) receptors and alpha-2 ( $\alpha$ 2) adrenoceptors. DEX is unique in that it may provide neuroprotection against apoptosis, ischemia, and inflammation while maintaining neuroplasticity, all while being readily administered, distributed, and removed from the body. DEX is unusual among anaesthetics in that it has the ability to avoid the neurotoxicity that is sometimes linked to anaesthesia because of this feature [47].

DEX may be a neuroprotective drug since preliminary evidence indicates that it protects against brain injury from ischemia-reperfusion (I/R), traumatic brain injury (TBI), subarachnoid hemorrhage (SAH), and cerebral ischemia. In the end, we discovered that DEX's neuroprotective effects mostly comprised five mechanisms: increase of stable cell structures, preservation of the blood-brain barrier, decrease of apoptosis and autophagy, and control of inflammatory responses. Thus, for individuals suffering from brain injuries, DEX can offer a significant benefit in their neurological recuperation [48]. According to recent research, DEX protects a number of organs. DEX may prove to be an innovative neuroprotective treatment for a variety of neurological conditions [49].

DEX has been shown to have anti-inflammatory properties by modulating inflammatory responses in the brain. It can reduce the release of pro-inflammatory cytokines and inhibit microglial activation, which plays a crucial role in neuroinflammation associated with neurological insults [50]. DEX holds promise as a neuroprotective agent through its various mechanisms of action, including anti-inflammatory, anti-apoptotic, antioxidant, and cerebrovascular effects. Further research is needed to elucidate its precise mechanisms and establish its efficacy in clinical settings, but it represents a potentially valuable therapeutic option for mitigating neurological damage in various pathological conditions.

#### **DEX as an Analgesic**

The study assessed the analgesic effectiveness of intraoperative dexmedetomidine (DEX) in treating acute postoperative pain in patients with colorectal cancer having laparoscopic surgery. During surgery, the DEX group had a lower minimum alveolar concentration of sevoflurane. There was no difference in pain levels or opioid intake across the groups on the first three postoperative days. There was no variation in the frequency of postoperative complications among the groups. Lower hemodynamic and fentanyl consumption were indicators of an intraoperative analgesic benefit from continuous intraoperative DEX injection [51].

Patients who received DEX infusion had a significant longer time to rescue analgesia compared with those without DEX co-administration. Although the visual analogue score appeared to decrease with DEX therapy, there was no statistically significant difference in the significance. DEX did not lengthen the duration of sensory block or lessen the time to reach the maximal degree of

sensory block when used as an analgesic adjuvant. The rate of hypotension was much higher with DEX treatment. As a result, rescue analgesia following femur fracture surgery lasted longer when DEX was used as a local anaesthetic adjuvant. But among these individuals, the frequency of hypotension was much higher [52]. DEX infusion was linked to a reduction in the amount of morphine used after surgery, a decreased risk of experiencing severe pain after surgery (odds ratio, and a noticeably longer period before using rescue analgesia for the first time. During and after elective LC, intraoperative DEX infusion improves analgesia in a safe and efficient manner [53].

A common treatment used to reduce postoperative pain after total knee arthroplasty (TKA) is periarticular infiltration analgesia (PIA). The analgesic effect in the early stages after TKA may be amplified and prolonged by adding DEX as an adjuvant to PIA without raising the risk of side effects [54]. Real-time non-invasive nociception monitoring was used to assess the analgesic effectiveness. Hypoxemia incidence was considerably lower in the DEX group. The blood pressures of the DEX and midazolam groups did not differ significantly. Additionally, postoperatively, the DEX group consumed less analgesic and had a lower maximum visual analogue scale score. When used systemically as an adjuvant medication, DEX has an independent analgesic effect and is more effective than midazolam in relieving pain without causing serious adverse effects [55]. DEX hydrochloride demonstrates robust analgesic properties through its modulation of central pain pathways and synergistic interactions with other analgesic medications. Its versatility and safety profile make it a valuable component of multimodal analgesic strategies in perioperative and critical care settings.

#### **Pharmacoeconomic Analysis of DEX**

A subfield of health economics called Pharmacoeconomics studies how to use medications in the most cost-effective and efficient ways possible. The costs and results of pharmaceutical goods and services are identified, quantified, and compared in pharmacoeconomic research. When it comes to the effective distribution of resources in healthcare systems with limited funding, pharmacoeconomic assessment can be quite important. Nations are attempting to manage the increasing expenses associated with health care due to their ageing populations. They're all asking the same thing: Is the new medication worth its price, and if so, how much will society be ready to pay for it? [56]. In healthcare systems with limited funding, economic assessment can be crucial to the effective distribution of resources [57]. To some extent, these days, resource distribution choices in a number of nations are subject to economic data. The primary responsibility of nearly every European country is the economic assessment of pharmaceuticals, carried out by some kind of committee or institute.

The reason for the rise in drug prices over time is that drug manufacturers' development costs have increased as a result of stricter regulations imposed after the thalidomide tragedy to protect the public from drug abuse. Additionally, the cost of manufacturing drugs is expected to rise due to new approaches to drug design and the development of new types of drugs using biotechnology. These surges in drug costs have forced multinational drug companies to raise the prices of their successfully marketed drugs in order to recover their high investment [58].

The costs and consequences of different pharmacological products

are identified, measured, and compared in pharmacoeconomic research. It makes use of various techniques and instruments to investigate the effects of complementary and alternative medicine treatments. Numerous fields, including economics, medical epidemiology, pharmacy, and social sciences, are used to inform research methodologies such as cost-effectiveness, cost-utility, and quality-of-life assessments [56]. In a cost-benefit analysis (CBA), every benefit that arises from the programme or intervention is identified and expressed as a monetary value for the year in which it occurs. Next, using the chosen interest rate, this benefit flow expressed in dollars is discounted to its equal present value. Concurrently, and on the other hand, every programme expense is determined, allotted for a certain year, and discounted to its present value. In terms of economic value, the programme with the highest present value of benefits at the lowest cost is the best one, assuming all relevant variables stay the same [59]. The term "cost-effectiveness analysis" (CEA) refers to a set of mathematical and analytical techniques that help choose a course of action among several possible strategies. This method works best when the program's results are easily quantifiable in monetary terms, but it's also suitable to express the results in terms of the health benefit that was achieved (e.g., life-years gained (LYG), time to event, greater survival rates, or faster clinical cure). A program or intervention if it has a high benefit (effectiveness)-to-cost ratio may not be appreciated equally by all members of the community, according to cost-benefit or cost-effectiveness analysis [60].

The effectiveness of DEX against esmolol in reducing the sympathomimetic reaction to laryngoscopy and intubation in patients undergoing elective neurosurgery was examined. After inducing anaesthesia for two minutes, all of the medications were injected during a ten-minute period. For elective neurosurgical patients, DEX 1 µg/kg is more effective than esmolol at reducing the hemodynamic response to laryngoscopy and intubation [61].

The fundamental idea of pharmacoeconomics is the cost of medication therapy and its potential benefits in relation to those expenses. An understanding of how to use and distribute financial resources in the healthcare system in a reasonable manner is gained by evaluating such concepts. This makes this facet of pharmaceutical science crucial. By carefully balancing cost and benefit, it may greatly aid in addressing the financial issues facing the healthcare system. It also facilitates the economic assessment process for clinical trials of novel medical goods and aids in the formulation of health-related policy decisions. Four methods of economic evaluation fall under the umbrella of pharmacoeconomics: cost-utility, cost-minimization, cost-benefit, and cost-effectiveness analysis. The sort of analysis used is determined by the specific conclusion needed for the context in which it is done and the context itself [62].

### **Prolonged Effects of DEX**

The active ingredient DEX is widely used in clinical practice as a sedative and analgesic. It is an alpha-2 adrenoceptor agonist, which results in the inhibition of the release of excitatory neurotransmitters. Furthermore, by activating the alpha-2 adrenoceptor in the central nervous system, DEX acts on the 'rest and digest' response, causing both sympatholytic and vagal effects. The literature describes how the long-term use of DEX in patients who are critically ill may contribute to improved outcomes such as a reduction in mechanical ventilation duration, length of stay, and delirium. This is reflected in our study results after conducting

long-term evaluation on patients with repetitive and frequent microneedling sessions. The grouping for the long-term effect achieved was similitude to the short-term effect evidence, but it was in general that the long-term treatment with the microneedling with DEX hydrochloride also significantly increased the collagen content because of the more collagen deposition overtime, which not only increase skin tightness but also make the skin figure. The collagen formation and the collagen content analysis have provided enough evidence and supported the claim of the long-term effect of microneedling that the length of the collagen bundle and the collagen content have significantly increased after the long-term treatment. However, it is worth to obey that the collagen formation is not immediate, and it requires time to form; in our literature view, several studies have used western blot and immunohistochemistry staining which was in both the gene and protein level. The vascular endothelial growth factor (VEGF), which is an important angiogenic factor, has been shown and proved that it has significantly increased after the microneedling hydrochloride treatment. Also, the hilar vessel presented in both the short-term and the long-term treatment, in both the meaningless and control achene. These statistical evidences for the long-term treatment are support the claim that microneedling would provide a long-term effect for the collagen induction therapy. The study demonstrated that the DEX group increased were larger than the control group, which indicated that the micro injury caused by the microneedling process has stimulated the collagen formation, according to the statistical results. It reflects the long-term effect and also the self-sustaining stability of the process in achieving the ultimate goal, which is to reduce the visible wrinkles and to get the tightness of the skin. These findings are supported by several literatures and studies that establish the biological effects in paragraph 3.3: long-term effects of microneedling.

### **Challenges to Pharmacoeconomic Studies**

Even though pharmacoeconomic assessments have potential benefit, utilising one of the aforementioned techniques for advice does not guarantee that decision-making will improve right away. It is important to remember that these tools are only as good as the data that went into creating them, thus it is ideal to utilise these analyses in conjunction with other tools when evaluating the effects of medical interventions [63]. Furthermore, in a cost-benefit analysis, each benefit is valued according to the person's maximal "willingness to pay" (WTP). The most amount that a person would be willing to give up, pay, or swap for a thing is known as their WTP. Projects are deemed worthwhile when the overall advantages surpass the whole expenses. Either the maximum WTP per unit of health gained or the cut-off suggested by the maximum budget might be utilised as a criterion [64].

The pharmaceutical and medical communities are now more aware of the price and efficacy of medications due to the increase in healthcare spending worldwide. The examination of healthcare products and services that are already accessible goes well beyond a simple assessment of their safety; it also takes into account the financial implications for healthcare budgets and cost factors. It is essential to execute economic efficiency through the fair use of pharmacoeconomic analysis and strategies for their implementation in order to use medical resources effectively [65]. Cost analysis studies have become an increasingly important developing subject due to the efforts of pharmaceutical analysts and practitioners. It addresses the financial and economic aspects

of the medical field with the goal of assessing the expenses and effects of medical goods and services on specific patients, the pharmaceutical industry, and entire healthcare systems. The increasing frequency of illnesses has led to an endless need for healthcare equipment, necessitating greater investment in its provision. This has a negative impact on public healthcare budgets in general and pharmaceutical businesses in particular. The difficulty of delivering high-quality medical treatment at the lowest possible cost highlights the significance of pharmacoeconomics [66]. The lack of consensus about the benchmark value (threshold) for a cost-effectiveness ratio and the best way to limit the provision of healthcare to patients whose ratios are higher than this is one of the main obstacles facing pharmacoeconomic research. Moreover, there is disagreement on how to make a choice when only low-quality data is available and how to account for outcome uncertainty in the decision-making process [58].

In previous research, other microneedling products use general anesthetic and thus clinic-based microneedling treatments have a good safety profile with a low incidence of significant adverse events. For example, a meta-analysis of the literature found that the most common adverse event noted was skin irritation/erythema, but that this was of 'mild severity'. Also, previous research has shown that products containing fully synthetic sequences used in microneedling technologies may avoid the risk of potential product variability come with naturally derived or human/animal-based products, such as those which contain growth factors and peptides. For example, there are variable levels of product quality and impurities which may be introduced due to the use of human/animal-based materials extracted from differing sources. Also, it has been found that the use of fully synthetic products may be preferable in obese patient groups due to improved resonance found with molecular stiffness; this is important in relation to help ensure a physically constructive energy is efficiently delivered to the surrounding cellular environment to promote tissue repair and remodeling. This works on the basis that molecular stiffness, or the force-displacement relationship of the molecular building blocks of materials, such as those found in skin membranes, dictates the transmission of mechanical forces within and between cells. This area of potential future use of the product is something that has been discussed with the product manufacturer as a proposed iterative design concept, and they have stated that their ongoing research and product development strategy is investigating the design of products that may be suitable for use across a wider range of patient indications. It is stated that the manufacture of microneedling products should adhere to good manufacturing practice and guidance set out by international and national standards, and that various standardizations are in place to ensure that appropriately high quality and safe products are produced for public use. These standards specify criteria that must be fulfilled by manufacturers in respect of materials, design, production, packaging, and, importantly, sterility and bio-contamination control. Also, as set out by the legislation, any prospective manufacture and placing of microneedling products on to the market within Europe must follow the medical devices regulatory framework that has been established under Directive 93/42/EEC; the essential principles of safety and performance requirements in providing health not only to humans themselves, but also to other persons and fundamental requirements of hygiene and health protection against infectious and transmissible agents are key

criteria in the design and regulation of microneedling devices. Further to this, a CE mark whereby the product has been assessed to meet European Union laws for the health, safety, and environmental requirements for medical devices is evidence that the product complies with this framework and that it has undergone verification, testing, and product quality monitoring as required. Also, it is noted by the product manufacturer that the clinical and laboratory research directions aim to demonstrate the long-term reliability, effectiveness, and safety profile of the product.

### Conclusion

Our study has reported that all groups showed positive growth in per capita medicine volume, medicine sales, total pharmaceutical counting units and averages sale price and package weight for the highest-selling therapeutic classes. The mean satisfaction score for all of the clinics indicated that most patients were highly satisfied with their treatment. Patient satisfaction and patient confidence ratings for microneedling were distributed highly towards confidence. The growing incidence of skin conditions, expanding knowledge of the advantages of microneedling, and rising expenditures in skin problem research and development are the main factors propelling the market for DEX. For several reasons, the market for microneedling and DEX has grown to be of utmost importance. Improvements in technology have rendered microneedling and DEX more revolutionary, influencing a variety of sectors, including manufacturing, transportation, and healthcare. Regulatory considerations focus on compliance with regulations, the approval process for microneedling products, and labeling and packaging requirements. Key drivers in the DEX market include increasing prevalence of skin disorders, growing awareness about the benefits of microneedling, and rising investments in research and development for treatment of skin disorders.

### Conflict of Interest

Authors hereby declare that they have no conflict of interest.

### Authors' Contribution

DK conceived and designed the study; analysed the results; wrote and revised the paper.

### Generative AI Statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

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