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Research Article

Numerical Simulation, Analysis, and Fabrication of MEMS-Based Solid Ag and Cu Microneedles for Biomedical Applications

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Microelectromechanical system (MEMS)-based devices have gained attention recently due to their beneficial biomedical applications. MEMS-based devices like microneedles have set new trends in drug delivery, vaccination, skin, and eye treatment. Different materials like metals, sugars, polymers, and silicon have been used for fabrication. Various techniques have been used for their fabrication, including laser ablation, lithography, injection molding, and additive manufacturing. The tip diameter of different micron ranges has been achieved. The strength and stiffness of the microneedle's tip have always been important in fabricating microneedles so that it does not break on insertion. This research paper presents a comparison between silver (Ag) and copper (Cu) solid microneedles by performing numerical analysis using the fuzzy approach, structural simulation, and fabrication. Firstly, structural simulation has been performed in ANSYS software to test the strength of silver (Ag) and copper (Cu) microneedles separately. The purpose is to compare the stress effect and fracture limit of both microneedles. The results collected from the simulation provide valuable target and prediction facts to fabricate improved designs of the solid Ag and Cu microneedles. Then, fuzzy-based numerical analysis has been performed in MATLAB software for both microneedles separately. In this numerical analysis, the effect on the range of microneedle tip diameter and cone length has been observed by varying input voltage and time. Finally, fabrication has been performed using a novel economical technique such as electrochemical etching. Electrochemical etching is a very low-cost and clean room-free technique as compared to other techniques used for the fabrication of microneedles. The fabrication technique adopted in this work is the same for both silver and copper microneedles. The scanning electron microscopy (SEM) characterization has been performed for both fabricated microneedle tips. The tip of the fabricated solid Ag and Cu microneedle has been then coated with drugs using the dip-coating method. The coated solid Ag and Cu microneedle's tip has been then characterized again using SEM. The numerical results calculated from the fuzzy analysis have been then compared with fabrication results. The fuzzy analysis gives the simulated size of the microneedle's tip for 5.05 μm silver and 5.12 μm copper which have very close approximation with the experimental values from the SEM micrographs which also give the values of the cone length from 400 to 500 μm and the tip size from 5 to 6 μm for the time of 10–15 minutes, whose values were optimized by the fuzzy analysis. The results of this research provide valuable benchmark and prediction data to fabricate improved designs of the silver solid microneedles for drug delivery and other biomedical applications.

1. Introduction

Microelectromechanical system (MEMS)- based technology has been increasing swiftly in biomedical devices. MEMSs are micron range devices that are the root of many integrated and smart devices. Due to microelectromechanical systems-based technology, the fabrication of miniature-size devices has been increased. The increasing performance of medicinal devices has become achievable to meet the critical medicinal requirements. These requirements include controlled drug delivery with insignificant side effects, enhanced bioavailability, and healing effects. In biomedicine, MEMS-based devices integrated with microneedles, microvalves, micropumps, and microchannels have many important biomedical applications. Scientists are working on their development and improvement for many years and set new trends. MEMS-based microneedles range from a few micrometers to millimeters. These microneedles are different from hypodermic microneedles because they are in the micrometer to millimeter range and make drug delivery easier and painless [1]. The objective of MEMS-based microneedles includes painless and safe insertion of needles into the skin and skin retrieval after the removal of the microneedle. They are also used in drug constancy throughout manufacturing, delivery, and storage. For patients, they help result in less pain, irritation, and infection in the skin, in addition to drug effectiveness and safety [2]. By developing a base with strong technology and multiple demos of effective drug delivery, microneedles are composed to progress more into clinical practice. This allows better medical therapies, vaccinations, and other numerous applications [3]. Microneedles have been categorized into four different types: solid microneedles, hollow microneedles, coated microneedles, and dissolving microneedles. Each microneedle type has its unique trend and innovation [4, 5]. Solid microneedles are commonly used for skin pretreatment to upsurge skin porousness. Coated microneedles which are drug-coated dissolve easily into the skin. Dissolving microneedles include polymers-made microneedles that comprise a drug and completely dissolve into the skin. Hollow microneedles are used to infuse the drug into the skin deeply [6–8]. Solid microneedles are nowadays of more interest because of their use in skin treatment as well as drug delivery. They are sharp enough and pierce into the skin or scrape the skin to make holes. Drugs can pass through these holes for either limited effect of the drug in the skin or universal delivery after acceptance by skin tubes [9–11]. A drug-loaded patch is used to apply to the skin surface above the pores for straight transdermal drug delivery. A semisolid contemporary formulation can also be used, such as a cream, ointment, gel, or lotion, because it is mostly used in skin treatments [12, 13]. The solid microneedles fabricated using different techniques have been concentrated on providing an appropriate mechanical strength. This is achieved by considering the sufficient materials for microneedles and geometry and by increasing tip sharpness to reduce the force required for inserting microneedles into the skin [14–16]. Some of the most common techniques used for the fabrication of microneedles are laser ablation, additive manufacturing, injection molding, and lithography as shown in Table 1.

Different materials used nowadays for the fabrication of microneedles are silicon, nondegradable polymers such as photolithographic epoxy a methyl vinyl ether copolymer, polycarbonate, maleic anhydride, and polymethyl-methacrylate (PMMA), polyglycolic acid (PGA), and polylactic acid (PLA). Water-soluble compounds comprised of maltose, metals containing stainless steel, titanium, nickel, and tantalum are also used [25, 26]. Microneedles have been experienced on human skin, and the other drug delivery MEMS devices have shown potential in vivo and in vitro [27]. Garcia et al. [28] reported self-sterilizing dissolving microneedles patches loaded with nanosilver and fabricated from carboxymethylcellulose which is proficient in surpassing the growth of microbial pathogen at the insertion place. Chang et al. [29] reviewed the modern developments of solid microneedles by concentrating on the materials and techniques used for the fabrication of solid microneedles. Driven by the exceptional structures and efficient materials, these microneedle patches can deliver unique solutions for skin diseases, diabetes, overweightness, and ocular diseases, as well as quick diagnosis. Liu et al. [30] presented the innovative biomedical applications of microneedles made of polymers for therapeutic delivery or transdermal drug delivery and diagnosis. The present limitations, as well as future perceptions of solid microneedles made from polymer materials, were also provided. Moussi et al. [31] presented the new biocompatible 3D-printing technique for developing solid microneedles required for undetectable tissue dispersion and transdermal and intradermal drug delivery. Lee et al. [32] discussed the design and formation of current microneedles that were designed with intention of surpassing the biological barricades of nontransdermal drug delivery in oral, optical, vascular, and mucosal tissues. Bonfante et al. [33] described that there are different polymers materials used for the fabrication of microneedles. So, to understand which polymer material is more appropriate depending upon its mechanical properties, they presented a comparison of polymers. It was to improve the mechanical properties of fabricated microneedles for different biomedical applications. Chi et al. [34] developed a biomass-based chitosan-microneedle-array patch combined with smart receptive drug delivery for endorsing wound curing. Cai et al. [35] summarized the innovative technologies working for the integration of microneedles arrays or patches with definite living organisms together with miscellaneous viruses, mammal cells, bacteria, and so on. Dugam et al. [36] reviewed different fabrication materials and techniques to emphasize distinct advantages of microneedles in biomedical industries. The development and design of MEMS-based microneedles are powerfully dependent on the fabrication method. Many of the present microfabrication technologies have resulted from procedures settled to fabricate ICs. One of the most common and significant fabrication technologies is photolithography [37]. Others include soft lithography, chemical vapor deposition, and stereolithography. All of these techniques are quite expensive and require a complete setup of sufficient environment for performing experimentation [1]. Similarly, different materials are used in the fabrication of microneedles, and the most common are silicon and polymers. Silicon is mostly used as a substrate in the fabrication of microneedles patches. This is because silicon has some outstanding mechanical as well as electrical properties and it also provides a great possibility to integrate the circuits on the transducer's substrate. For stand-alone microneedles silicon, metal, and polymer materials are greatly used in the fabrication of these stand-alone microneedles. Each of these

Table 1: Microneedles fabrication techniques.

Fabrication techniques	Overview	Cost analysis/disadvantages	References
Lithography	The master pattern of the geometric shapes transfers to the substrate surface	High cost not suitable for mass production	[16, 17]
Additive manufacturing/surface micromachining	Layer-by-layer microneedles printing	Cost-effective but not too	[16, 18, 19]
Injection molding	Inject plastic materials into a mold	High initial cost (machine equipment is costly). Composite processes	[1, 20, 21]
Laser ablation	Use laser beam for making the substrate on which microneedles are fabricated	High cost not appropriate for large manufacturers	[22–24]

materials has its strength and efficiency [38]. Silver material has been used as a coating material for microneedles. They are fabricated from other materials and loaded as nanosilver in dissolving microneedles. Silver material is a renowned antimicrobic agent in contrast to an extensive range of microbes, over 650 microbes from diverse classes, that is, Gram-positive and Gram-negative bacteria and viruses. Owing to the ratio among positive and negative side effects, silver has advantages over numerous other antimicrobic agents and particularly antibiotics [21, 39]. Silver has an interesting history of using antibiotics in human well-being. It has been industrialized for usage in water sanitization, wound cleaning, bone prosthetic device, rehabilitative orthopaedical surgical procedure, cardiac care, and surgical applications. Progressing biotechnology has allowed integration into fabrics of ionizable silver for clinical uses to cut the risk of infections as well as for individual hygiene [40]. The antimicrobic action of silver/silver compounds is relational to the bioactive silver ion and its accessibility to interrelate with microbial or fungous cell membranes [25, 41]. Silver metal or inert silver compounds ionize in water, other specimen fluids, or tissue exudations. The silver ions are organically active and voluntarily interrelate with proteins, amino-acid remains, free anions, and receptors on mammals and eukaryotic cell membranes. The bactericidal action of silver is well known. It helps in reducing or avoiding contamination. It can be seen in numerous applications such as treatment for injuries and wounds that are chronic and as a coating layer for both momentary and permanent medicinal devices. Silver has been extensively used as a nanoparticle in many types of research. Silver nanoparticles have many potential applications that are highly influenced by a few factors such as shape and size [42, 43]. Many types of research have been done on silver nanoparticles and nanowires due to their tremendous applications [44]. Silver material has not been used for microneedles fabrication; however, coating with silver has been done on microneedles. It is fabricated from other materials and loaded as nanosilver in dissolving microneedles. Silver material is a renowned antimicrobic agent in contrast to an extensive range of microbes, over 650 microbes from diverse classes, such as Gram-positive and Gram-negative bacteria and viruses. Owing to the ratio among positive and negative side effects, silver has advantages over numerous other antimicrobic agents, particularly antibiotics. Silver has an interesting history of using antibiotics in human well-being. It has been industrialized for usage in water sanitization, wound cleaning, bone prosthetic device, rehabilitative orthopaedical surgical procedure, cardiac care, and surgical applications [45, 46]. Progressing biotechnology has allowed integration into fabrics of ionizable silver for clinical uses to cut the risk of infections as well as for individual hygiene. The antimicrobic action of silver/silver compounds is relational to the bioactive silver ion and its accessibility to interrelate with microbial or fungous cell membranes. Silver metal or inert silver compounds ionize in water, other specimen fluids, or tissue exudations [47, 48]. The silver ions are organically active and voluntarily interrelate with proteins, amino-acid remains, free anions, and receptors on mammals and eucaryotic cell membranes. The bactericidal action of silver is well known. It helps in reducing or avoiding contamination. It can be seen in numerous applications such that treatment for injuries and wounds that are chronic and as a coating layer for both momentary and permanent medicinal devices. Silver has been extensively used as a nanoparticle in many types of research [49, 50]. Silver nanoparticles have many potential applications that are highly influenced by a few factors such as shape and size. Many types of research have been done on silver nanoparticles and nanowires due to their tremendous applications [51]. Silver material has not been used for microneedles fabrication; however, coating with silver has been done on microneedles. On the other hand, copper-based hollow microneedles have been fabricated so far using electrodeposition-based additive manufacturing techniques. Copper has been used for plating different metal microneedles. Copper nanoparticles have been fabricated for many years using the natural process of chemical synthesis [52–54]. Copper acts as an antibiotic, antifungal, and antimicrobial agent when added to coatings. Copper has many biological applications which make researchers use copper in developing copper-based biomaterials. These biomaterials exhibit exceptional properties in protecting the cardiac system, helping bone fracture healing, and employing antibacterial effects [55–60]. In this research, we have fabricated solid silver and copper microneedles by using an economical technique of electrochemical etching. But, before fabrication, simulation of MEMS-based microneedles has been performed. Simulation is the best way to optimize the model and process parameters before fabrication. Many simulation tools are used nowadays including COMSOL, ANSYS, and Matlab. It has been identified that, by using fuzzy tools and intelligent systems, better results were achieved. These fuzzy systems have valued logic between integers of 0 and 1. Many researchers have used fuzzy logic for monitoring and optimizing their fabricated products and done marvelous work in their research areas [61–66]. Here in our research multiple simulations using fuzzy numerical analysis have been conducted to optimize the effect of input parameters of time, voltage, and elastic modulus on the output of tip diameter and cone length. For structural simulation and fluidic analysis, ANSYS software has been used. Zhang et al. [67] performed finite element analysis of out-of-plane microneedles using ANSYS for transdermal drug delivery. Ashraf et al. [68] conducted simulation by using ANSYS before fabrication to optimize the suitability of design for transdermal drug delivery. Kuo et al. [69] conducted a numerical simulation to confirm the design of PLA microneedle using the optimal process parameters. In our research, ANSYS has been used to check solid silver and copper microneedles' tip strength and how much force or stress they will bear when inserted into the skin. After that fabrication has been performed using the electrochemical etching technique. The fabricated microneedle tip has been then sent for characterization using a scanning electron microscope (SEM). The fabricated microneedles tip has been then coated with drugs. The coated tips have also been characterized using SEM (scanning electron microscope). The surface of solid microneedle's tip before and after the coating has also been observed in SEM characterization to quantify the amount of drug coating onto the microneedle tip depending on its surface tension, capillary forces, and viscous forces.

2. Structural Simulation

MEMS-based microneedles are usually patterned as an array on the patch which is just like the nicotine patch or hydrogel patch used in baby diapers. But here, for a better understanding of the structure and working of the MEMS-based microneedle, we just assume a single microneedle made of silver and copper materials. ANSYS workbench has been used for simulation on which step-by-step simulation is carried out. The simulation for both silver and copper microneedles has been performed separately. First, the 3D model of microneedle has been designed. Afterward, the force has been applied on the designed microneedle to estimate how much force or stress it can bear when applied to the human body. In this structural examination, a microneedle with 500 μm length, 200 μm width, and approximately 5–7 μm tip diameter has been designed in the design modeler of ANSYS workbench. The 3D and meshed model of the designed microneedle is shown in Figure 1. Afterward, the designed 3D structure has been meshed using a mesh tool available in the ANSYS workbench because ANSYS is a finite element analysis (FEA) software and by meshing the structure we can do an element-by-element analysis of 3D structure. After designing the 3D model and analyzing the mesh model for silver and copper microneedle. The different parameters of mechanical properties such as Young's modulus, elastic modulus, Poisson's ratio, ultimate tensile strength, compressive tensile strength, and density for silver and copper material have been assigned to estimate the endurance and strength of our final fabricated model. The boundary conditions of stress and fixed support are applied to analyze the effect of stress from tip to base when inserted on the human skin. The stress effect on designed 3D solid model for microneedle is shown in Figure 2. When the stress of 800 MPa is applied, it goes from top to bottom. It is because first the tip is being applied to the skin for drug delivery.

Then, simulation results of total deformation, directional deformation, von Mises stress, equivalent elastic strain, and structural error for solid copper and silver microneedle are shown in Figures 3–7.

The tip comparison has also been done to check how much deflection occurs when stress is applied. The change in deflection and deformation of both microneedles depends on their elastic modulus and how much elasticity or stiffness they have to overcome the stress. Thus, comparison of tip's deflection is shown in Figure 8.

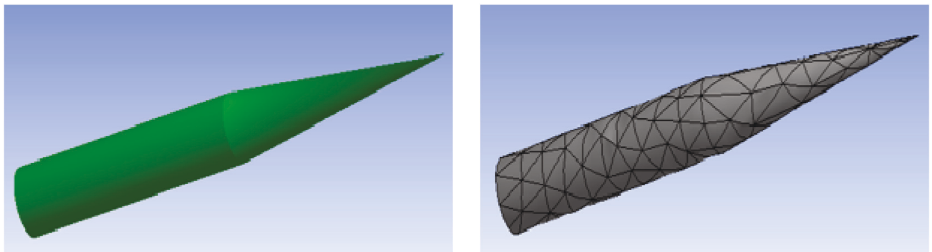
The results presented above have been taken by performing simulation in ANSYS workbench which is FEA software. Simulation is useful as it reduces the resources instead of direct fabrication.

3. Fuzzy Analysis

Fuzzy numerical analysis has been used to define the parameter of the systems in a definite way. The uncertainties and inaccuracies of physical systems can be easily quantified by using fuzzy numerical logic analysis. Appropriate notation, fractional truth concept, Boolean truth, and Boolean logic have been used in fuzzy numerical analysis to describe the accuracies of physical systems [70, 71]. Fuzzy numerical logic has its impact on every area of life and its application such as material sciences, MEMS-based devices [72], fluid dynamics, agricultural problems, information expertise, and automobiles and even in the advancement of control systems. In this research paper, numerical analysis performed by using fuzzy logic controller is presented. Fuzzy conditions are considered to be as accurate as the ideal conditions. They are more dependable as they can give infinite values in between zero and one.

It has been found in the literature that fuzzy logic has been used in many different appliances like blood pressure, washing machine, and other smart devices [73, 74]. Therefore, for understanding the effect of time, voltage, and elastic modulus on the tip diameter and needle length, we have also used fuzzy logic for analysis and consideration. The input parameters are time, voltage, and elastic modulus, whereas the output parameters are tip diameter and cone length. The microneedle FLC interface for both microneedles is given in Figure 9. Here, in both FLC models, three inputs have been considered and outputs have been achieved by varying the input conditions.

A fuzzy numerical-based logic controller has some important properties which include being easy to handle, flexibility of functional values, ease to understand, and easy modeling development, and, despite all this, it gives a



(a) (b)

Figure 1: Project design overview. (a) 3D model of solid microneedle. (b) Mesh view of the solid microneedle.

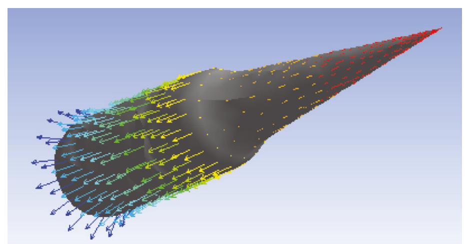
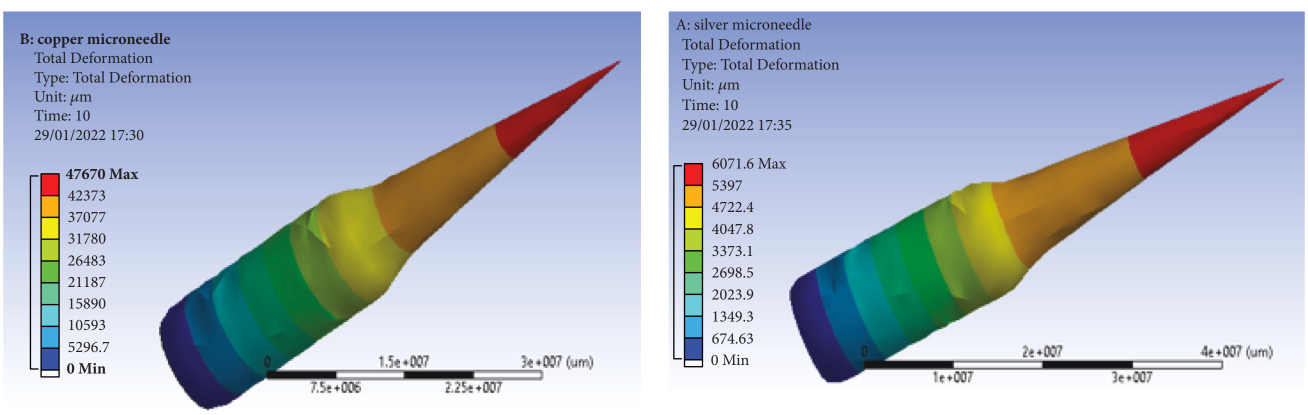
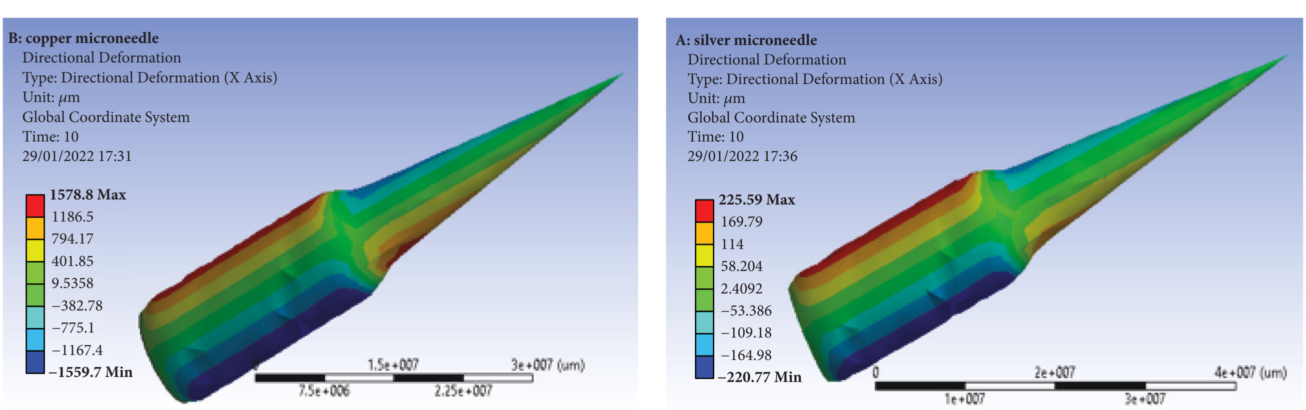


Figure 2: Stress effect overview on the 3D model of solid microneedle.



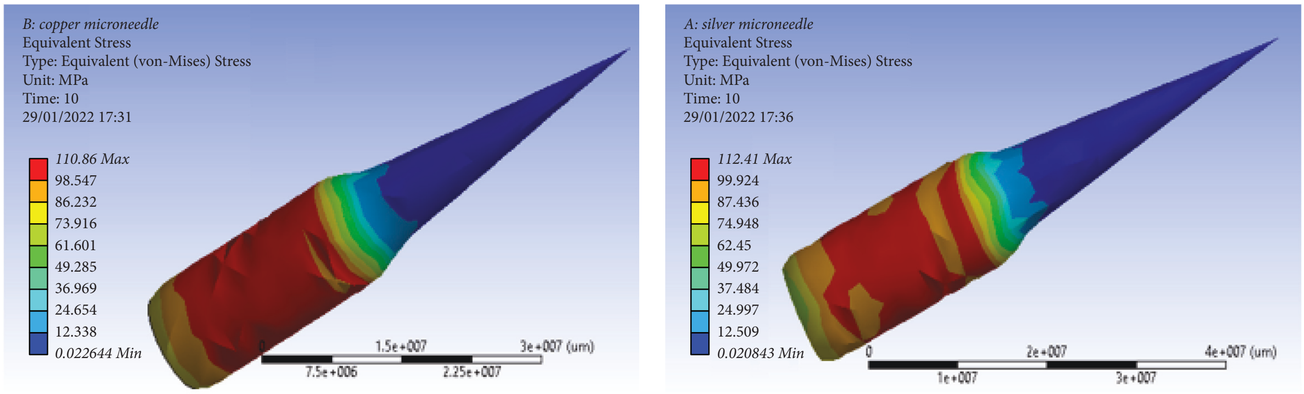
(a) (b)

Figure 3: Comparison between simulated results of total deformation for (a) copper microneedle and (b) silver microneedle.



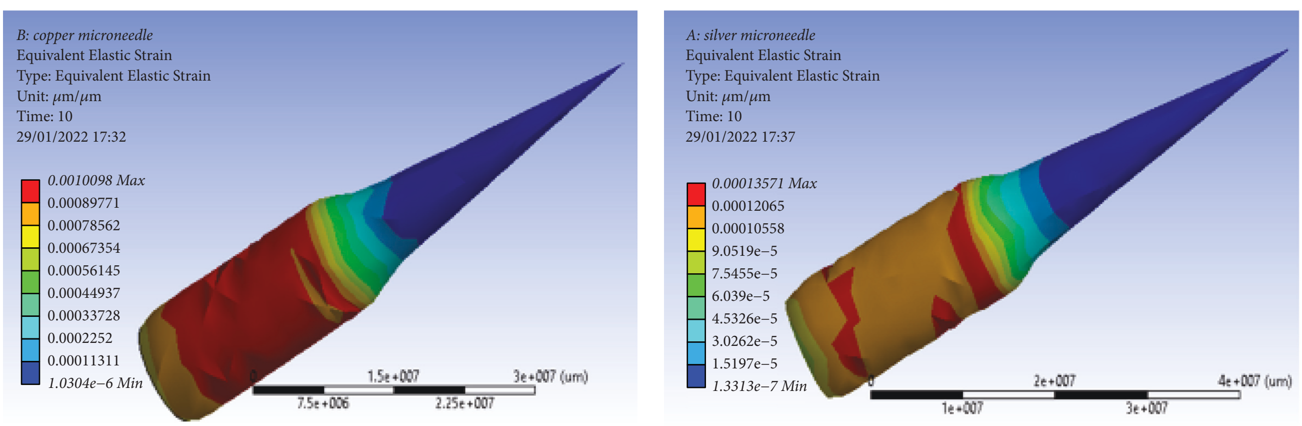
(a) (b)

Figure 4: Comparison between simulated results of directional deformation for (a) copper microneedle and (b) silver microneedle.



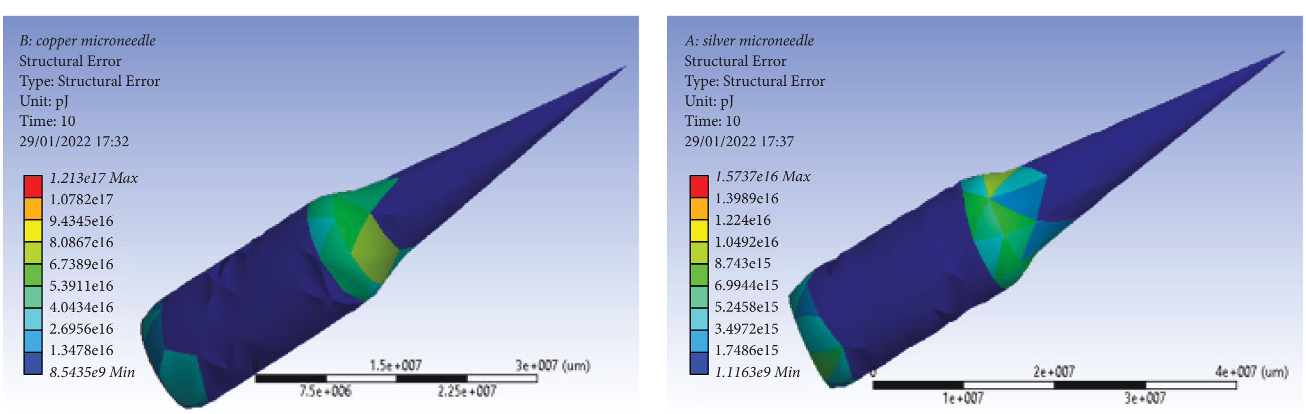
(a) (b)

Figure 5: Comparison between simulated results of Von Mises stress for (a) copper microneedle and (b) silver microneedle.



(a) (b)

Figure 6: Comparison between simulated results of equivalent elastic strain for (a) copper microneedle and (b) silver microneedle.



(a) (b)

Figure 7: Comparison between simulated results of structural error for (a) copper microneedle and (b) silver microneedle.

solution to the problem in big data systems due to Boolean manipulation [75]. In this research, simulations have been performed using fuzzy numerical analysis to optimize the process parameters. On the basis of these numerically optimized parameters, fabrication has been done to cut off extra expenses and get better designed fabricated model. The input and output parameters are designated by keeping all other parameters of the system constant. After deciding the

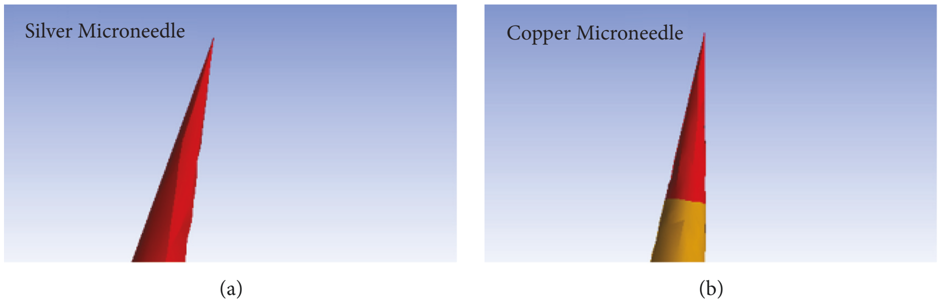


Figure 8: Comparison of tip's deflection when stress is applied. (a) Silver microneedle and (b) copper microneedle.

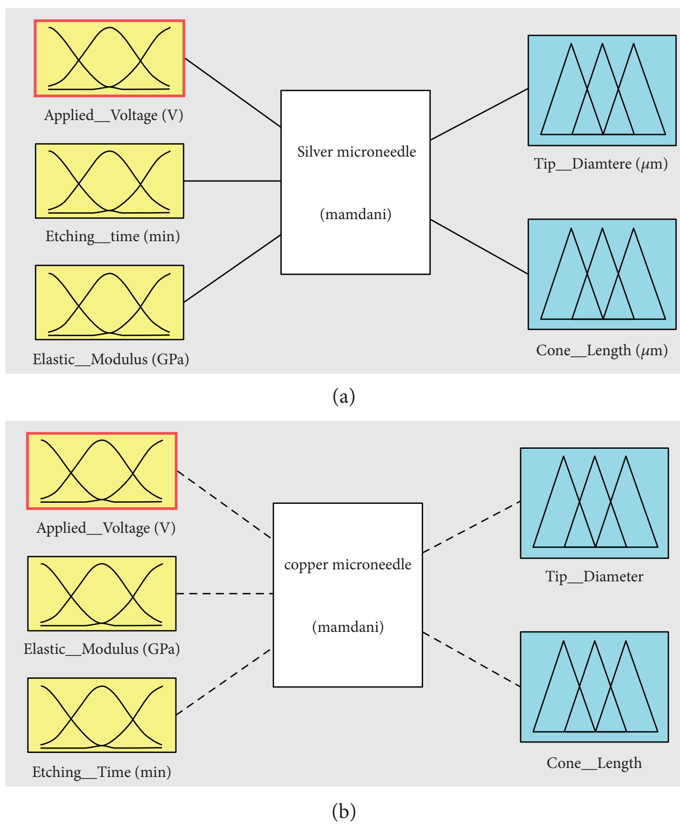


Figure 9: The microneedle FLC interface. (a) Silver microneedle. (b) Copper microneedle.

inputs and outputs, the membership functions for both parameters have been made by selecting the different ranges of values. The ranges of values chosen for membership functions are given in Table 2.

After that, the Mamdani model [76] has been used for the fuzzification of the MEMS-based microneedle by defining the all possible rules. The membership function plots for both microneedles are drawn and they are the same as inputs and outputs are the same for both. The inputs and outputs membership function plots are given in Figures 10–14.

In Figures 13 and 14, it is shown that the membership function values for outputs of tip diameter and cone length are small; possibly the best output deliberation is indicated by the red line in the membership function plots. After the fuzzification, the surface viewer has been drawn for both microneedles to explain in detail the comparative effect of input parameters values like voltage, time, and elastic modulus on the ranges of tip diameter and cone length for both silver and copper microneedles as shown in Figures 15–18.

Table 2: All inputs and outputs values.

Sr. no.	Inputs	Selected range
1	Applied voltage	0–30 V
2	Etching time	0–60 min
3	Elastic modulus	0–300 GPa
	Outputs	
1	Tip diameter	0–10 μm
2	Cone length	0–500 μm

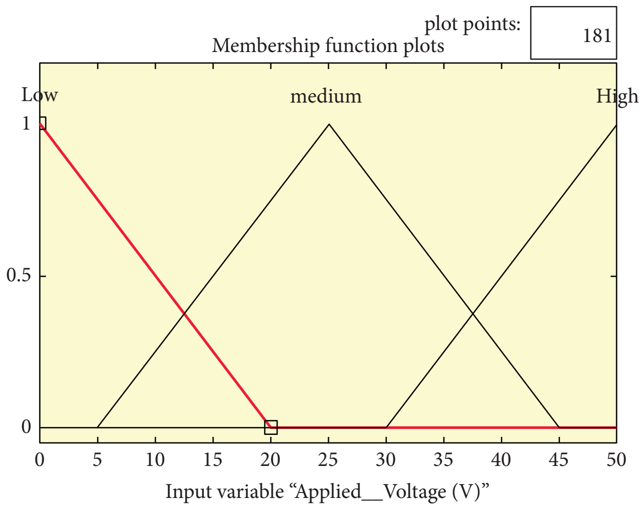


Figure 10: Membership function plot for applied voltage.

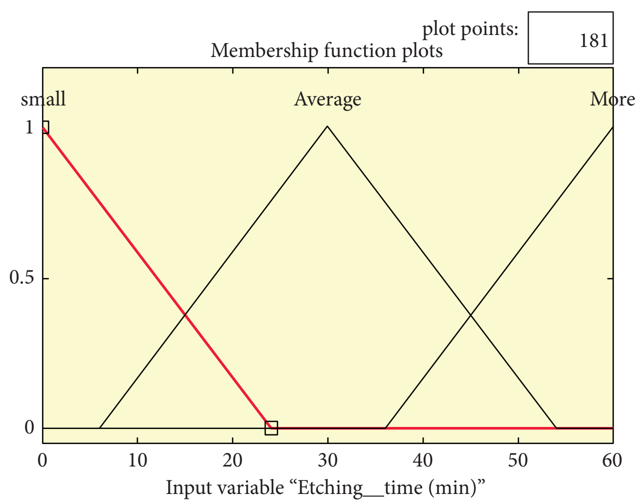


Figure 11: Membership function for etching time.

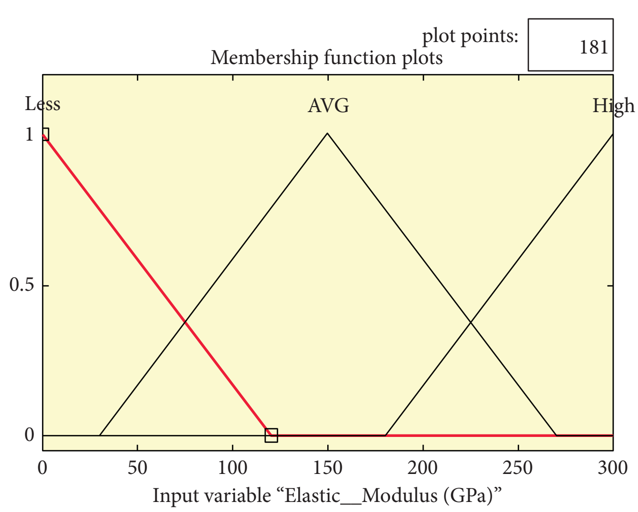


Figure 12: Membership function for elastic modulus.

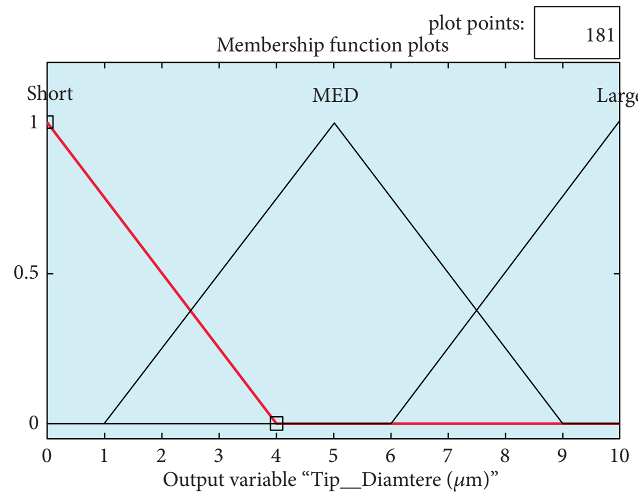


Figure 13: Membership function for tip diameter.

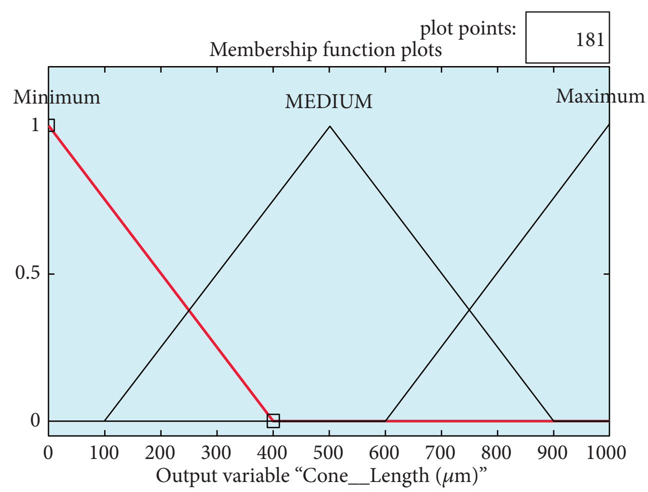


Figure 14: Membership function for cone length.

Figures 15–18 show the effect on tip diameter and cone length of fabricated Ag and Cu microneedles by varying applied voltage, elastic modulus, and etching time. It has been found that the tip diameter keeps decreasing around 5–6 μm when current and applied voltages increase. The cone length is maximum on the applied input parameters. The comparison of rule viewer for both microneedles calculated by FLC simulation on setting value range for both input and output parameters is given in Figure 19.

After the comparative numerical analysis of silver and copper microneedles using FLC, it has been found that using the same input parameters of applied voltage and etching time for both microneedles gives us tip diameters of around 5.05 μm for silver and 5.12 μm for copper with cone length of approximately 500 μm for both. These values for both tip diameters are obtained by varying input parameters of applied voltage and etching time with respect to fixed elastic modulus of both microneedles. It has also been observed in numerical analysis that, for copper microneedle, etching

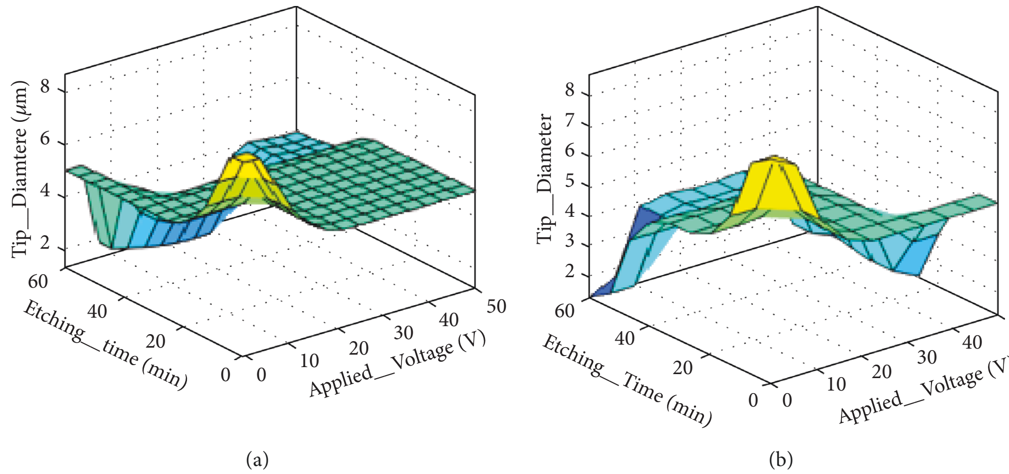


Figure 15: Comparison of the surface viewer of tip diameter with respect to etching time and applied voltage for (a) silver microneedle and (b) copper microneedle.

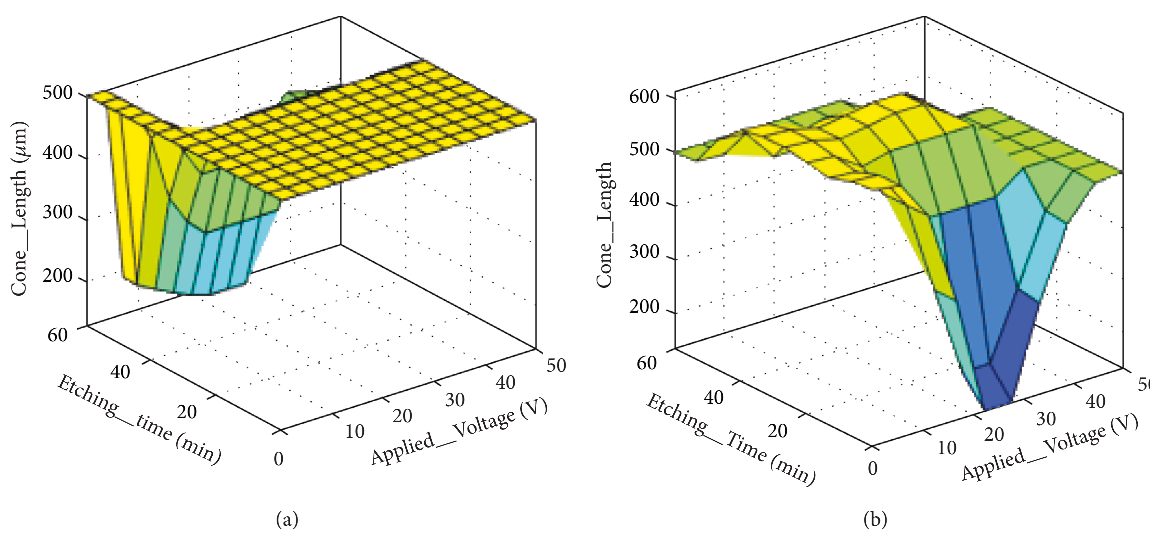


Figure 16: Comparison of the surface viewer of cone length with respect to etching time and applied voltage for (a) silver microneedle and (b) copper microneedle.

time and voltage need to be increased more as compared to silver microneedle etching. Also, it has been observed by surface viewer and rule viewer that, by increasing the applied voltage and etching time, the tip diameter decreases. The slight difference between the tip diameters of silver and copper microneedles is due to the elasticity of the materials. Copper is considered to have comparatively more elastic modulus and more stiffness than silver.

As the fuzzification of any device is based on the Mamdani model, here, for MEMS-based microneedle, the Mamdani model has also been considered. Some mathematical calculations have been done to understand the comparison between simulated and Mamdani values for both microneedles separately to calculate the accuracy or error percentage of our FLC simulation results. For the error percentage confirmation, Mamdani's formula has been used for the mathematical/numerical calculations. It has been found that a tip diameter of 5.13 for copper microneedle and a tip diameter of 5.06 for silver microneedle are obtained, whereas, from Mamdani mathematical calculations, the cone length for both microneedles was found to be about 498 μm. The difference between the fuzzy simulated values and the Mamdani mathematical values for microneedles' tip and cone length gives just 0.01% and 0.02% errors.

4. Fabrication Analysis

4.1. Materials and Methods for Silver Solid Microneedle. For silver solid microneedle, the etchant has been prepared by mixing the 3M solution of HCL and FeH18N3O18 into DI water. For this purpose, 30 g high graded ferric nitrate non-ahydrate (FeH18N3O18) has been mixed into the 250 ml DI

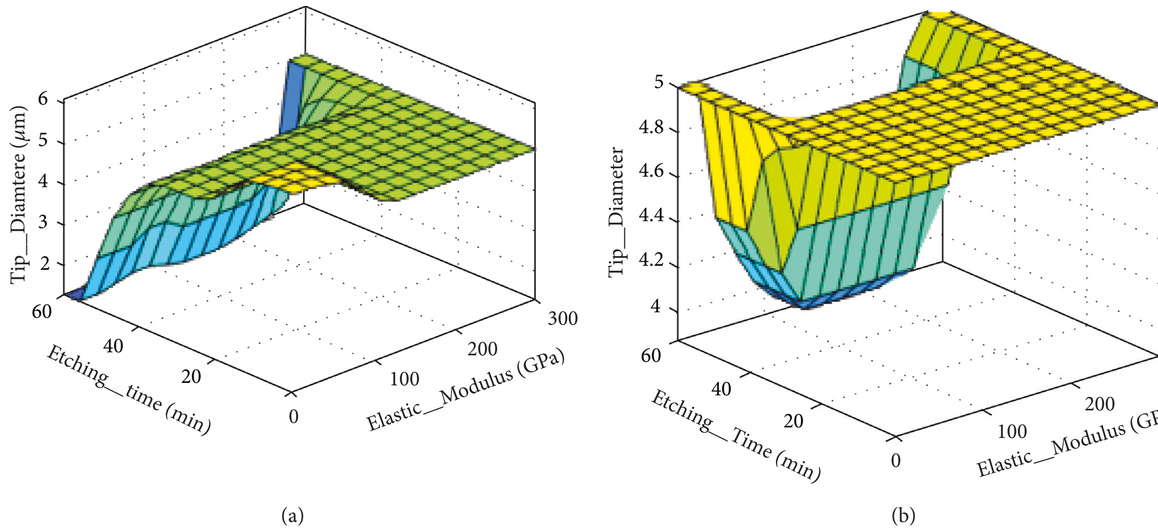


Figure 17: Comparison of the surface viewer of tip diameter with respect to etching time and elastic modulus for (a) silver microneedle and (b) copper microneedle.

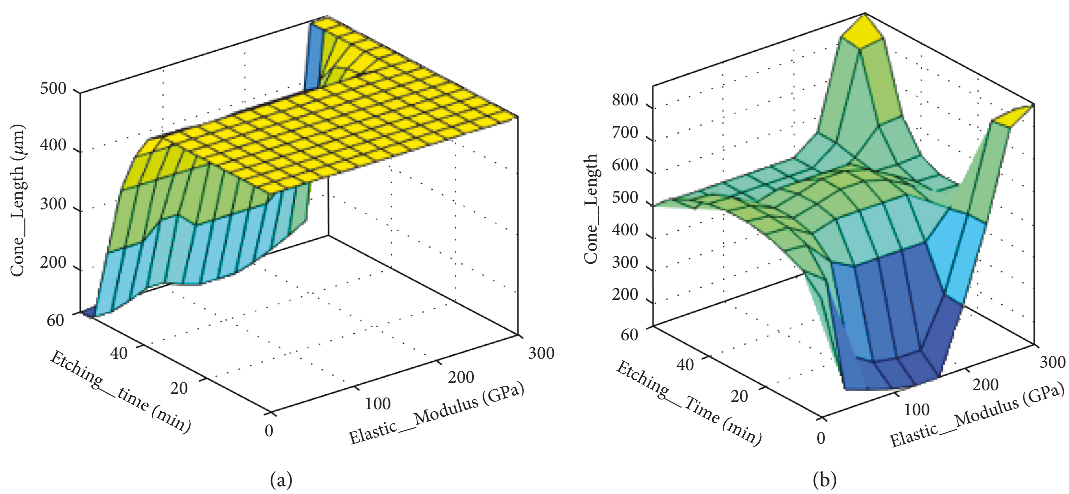


Figure 18: Comparison of the surface viewer of cone length with respect to etching time and applied voltage for (a) silver microneedle and (b) copper microneedle.

water and then magnetically stirred for 30 minutes. After stirring, 10 ml of HCl has been mixed dropwise into the former prepared solution which turned intense yellow immediately.

4.2. Materials and Methods for Copper Solid Microneedle. For copper solid microneedle, the etchant has been prepared by mixing the 3M solution of NaCl and HCL into DI water. For this purpose, 30 g high graded NaCl (Sigma-Aldrich 99%) has been mixed into the 250 ml deionized water (DI, Q-murk deionizer) and magnetically stirred for 20 minutes. After stirring, 10 ml of HCl has been mixed into the formerly prepared solution dropwise which maintained a light blue color.

4.3. Experimental Setup. For the fabrication of silver and copper solid microneedle, the self-designed setup has been used. The self-designed setup works on the principle of electrolysis and is named electrochemical etching. The experimental setup used for fabrication consists of the glass beaker which is round neck from the top (Pyrox, 500 ml) with a glass lid having a hole to let the graphite cathode and a catcher pass through it.

A catcher has been used for holding the silver and copper wire and it acts as an anode. Both wires attached to the catcher have been immersed into the etchant vertically with the help of the conducting catcher. DC power supply has been attached across the electrodes with the help of the probes. The voltage, time, and current have been controlled physically by the knob (used for tunning) attached to the power supply as shown in Figure 5. A pure silver (925 sterling) wire of 0.5 mm has been purchased and then cut into small pieces of 1.7–2 cm in length. Similarly, copper wire of fin quality has been purchased and then cut into small pieces of 1.5–2 cm in length.

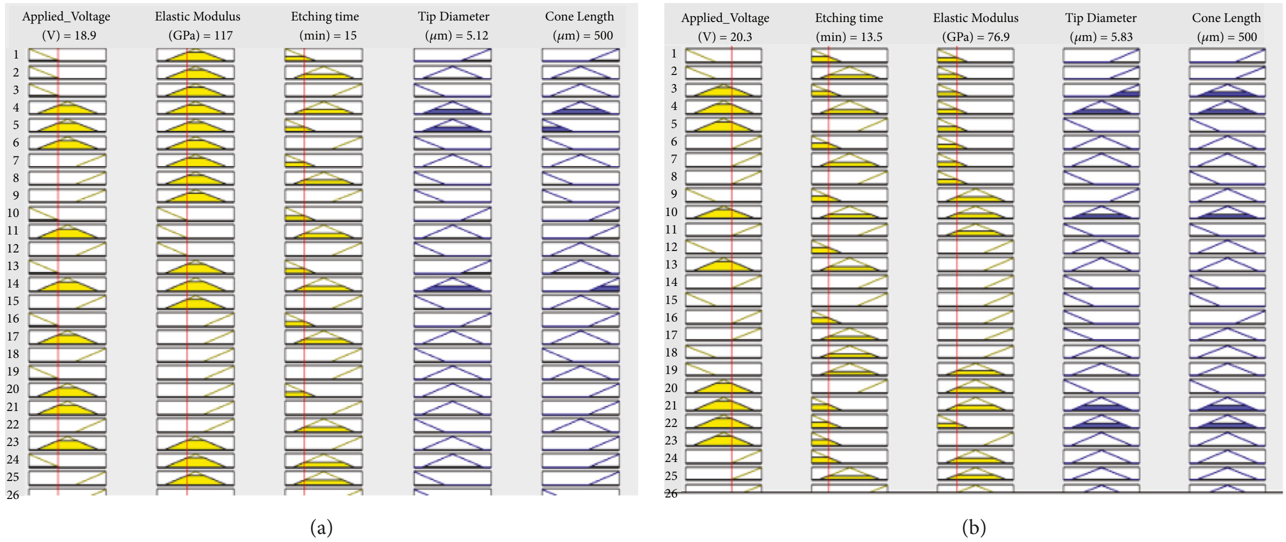


Figure 19: Rule viewer comparison for (a) silver microneedle and (b) copper microneedle.

4.4. Electrochemical Etching Procedure. After cutting, the silver and copper wires have been properly cleaned by the deionized (DI) water. Then, both cleansed wires have been placed into the ultrasonic bath for 20 mins to remove all impurities. Next silver and copper wires have been placed in the separate Petri dishes having ethanol and left for drying in the laboratory oven under the heat treatment at about 1500°C. After the cleaning process, the prepared etchant solution of electrolyte has been put into the glass beaker of the etching setup. The graphite cathode and cleaned silver wire and copper wire anode are dipped vertically into the separately prepared etchant solution for both microneedles. A DC of 30 mA and voltage of 15–24 V have been applied across electrodes for 10–20 minutes by using a regulated DC power supply for both microneedles. After etching is done, the silver and copper needles have been again washed by using DI water and ethanol. Finally, the fabricated silver and copper microneedles have been sent for characterization. The fabricated silver and copper microneedles have about 6 μm diameter. The schematic for electrochemical etching of silver and copper microneedles is shown in Figure 20.

The etching mechanism is also explained as shown in Figure 21 showing how the etching has been performed when the silver and copper wires were dipped into the prepared etchant solution.

5. Characterization Results

The fabricated silver and copper solid microneedles have been characterized after a thorough analysis by the scanning electron microscope (SEM). The tip of both microneedles has a range of around 5-6 μm. The SEM image has been taken for different micron ranges to observe microneedles closely. The SEM characterization for both solid microneedles has been performed to study the structure of microneedles.

The SEM results for both solid microneedles with cone length of approximately 500 μm are shown in Figure 22.

Also, the zoomed SEM images of both silver and copper microneedles have been taken to observe the etched surface of both microneedles' tips as shown in Figure 23.

6. Coating of Microneedles

After the characterization for silver and copper solid microneedle has been done, the coating of material on microneedles has been done. For coating, the dip-coating method has been used and prototypical molecules of riboflavin (7,8-dimethyl-10-[(2S,3S,4R)-2,3,4,5-tetrahydroxypentyl] benzo[g]pteridine-2,4-dione) has been coated on the microneedle. First, the microneedles have been dipped separately into 3 micrograms of riboflavin and then taken off. The microneedles entrain a liquid film on their tip surface upon exiting the coating liquid. The dissolved solids existing in the liquid film get deposited on the solid silver and copper microneedle surface as a coating after the solvent in the liquid film evaporates.

The contribution of surface tension of coating material is significant in the dip-coating method. The coated silver and copper microneedles have also been sent for characterization to quantify how many drugs coated on their surfaces hold, and comparative images with 2x zoom are shown in Figure 24 and Figure 25 before and after coating.

Also, the surfaces of coated microneedles have been observed for quantifying the amount of drug stuck on it as shown in Figure 25.

7. Results and Discussion

The graphical analysis has been done firstly on the simulation results taken for both silver and copper solid microneedles. The fracture strength of the microneedle's tip has been examined to evaluate the possibility of its fracture during the medical application. Therefore, how much tip deflection takes place on applying stress of around 800 MPa so that its fracture limit is being estimated has been analyzed

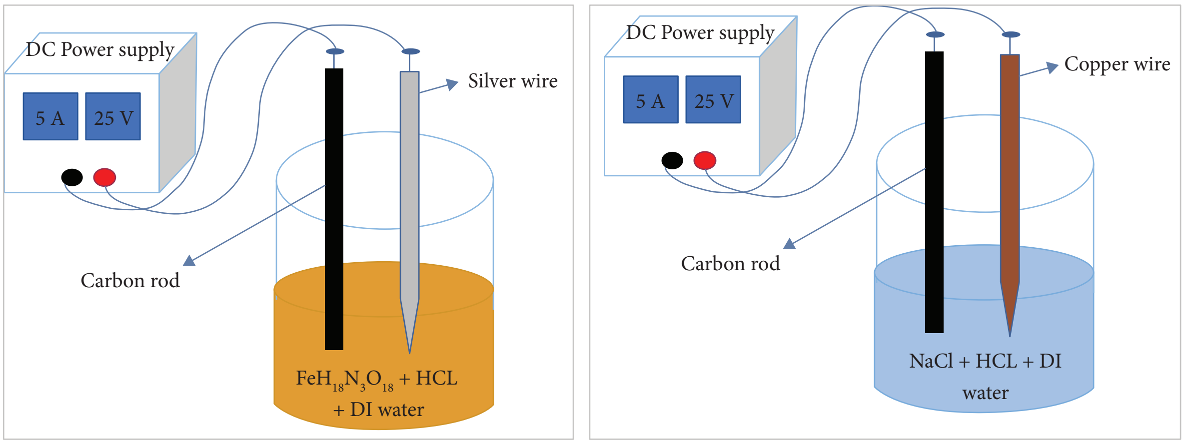
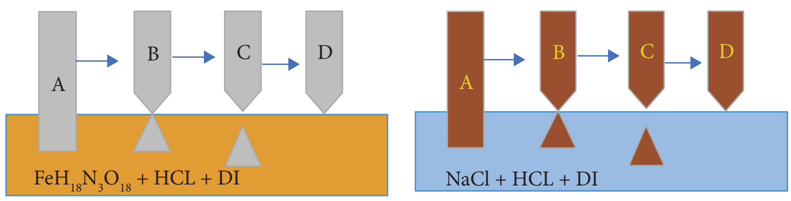
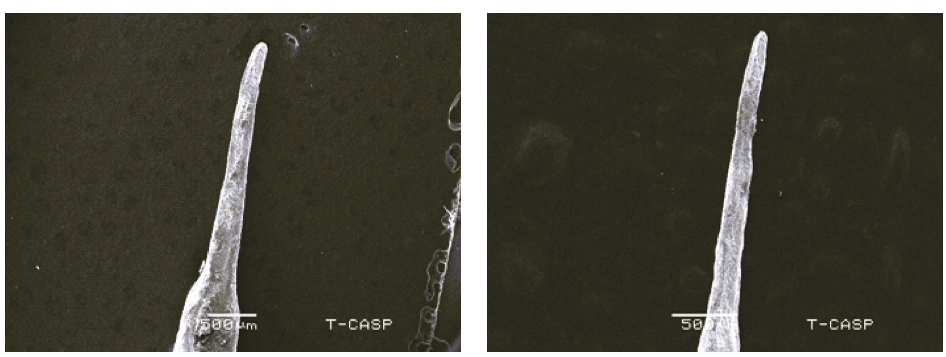


Figure 20: Schematic electrochemical etching setup for silver and copper solid microneedle.



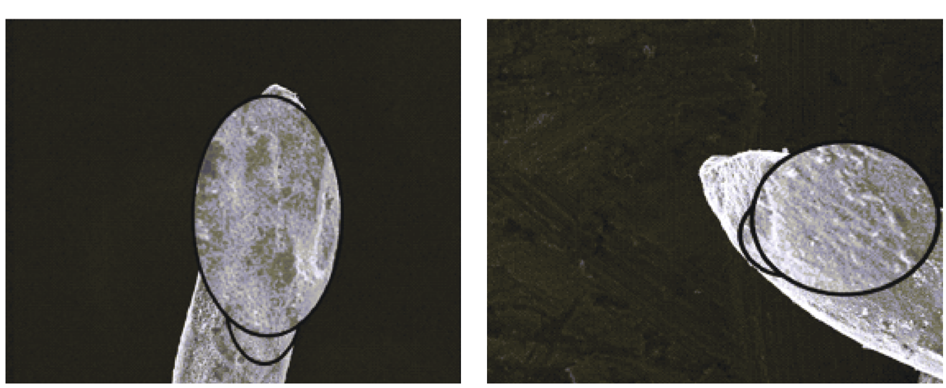
(a) (b)

Figure 21: Etching mechanism for (a) silver and (b) copper solid microneedles.



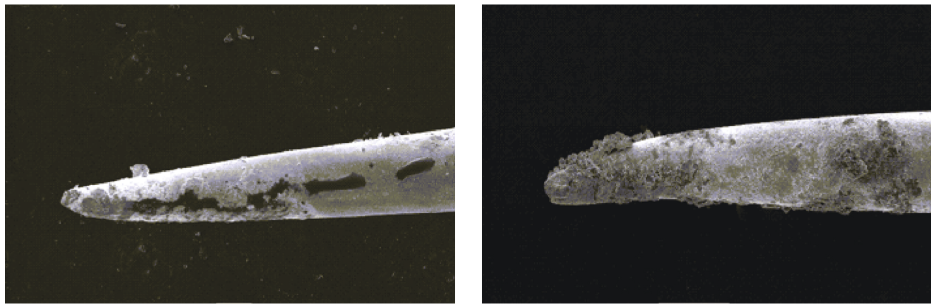
(a) (b)

Figure 22: SEM image of (a) silver and (b) copper microneedle tip for 500 μm.



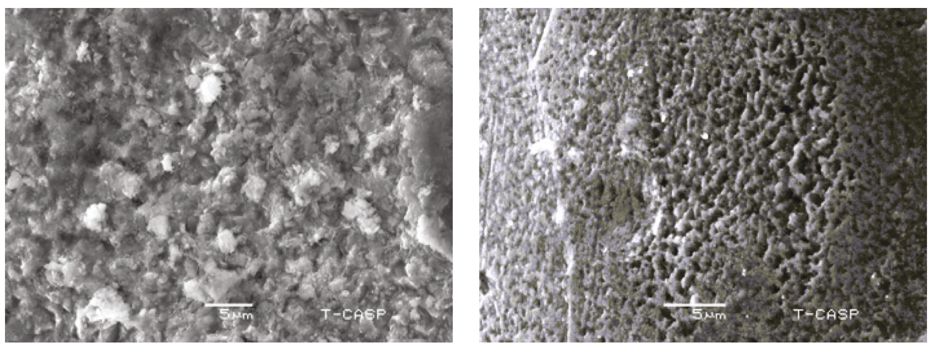
(a) (b)

Figure 23: 2x zoomed SEM images of (a) silver and (b) copper microneedle tips with a magnified etched surface.



(a) (b)

Figure 24: Magnified SEM images of (a) silver and (b) copper coated microneedle.



(a) (b)

Figure 25: Magnified SEM images of tip surface (a) silver and (b) copper coated microneedle.

because once the tip starts deflecting rapidly it is more likely to get fractured on the application. The tip deflection based on the stress-tip diameter data obtained from the simulation results are displayed in Figure 26(a), and fracture strength is in Figure 26(b).

It has been analyzed from the graph depicting the results of a structural simulation that fracture strength of silver microneedle is relatively low as compared to that of copper microneedle.

This is because silver has a comparatively less elastic limit and tensile strength than copper, and detailed properties are given in Table 3.

When microneedles are inserted into the skin, various forces like bending, buckling, resistive, compressive, and lateral forces have been influenced on microneedles. To predict the effect of these various forces for the projected design, the structural analysis has been executed in ANSYS. In structural analysis, the total deflection along the length of both silver and copper microneedles at the applied force of 10 N is shown in Figure 27.

In this graph, it has been observed that when force is applied a deflection starts at the length of approximately 100 μm for both solid microneedles.

In fabrication, two parameters of time and voltage have been set. By varying these two parameters, the effect on tip diameter has been analyzed and it is the same for both microneedles depending on the materials used for them. The graph is given in Figure 28.

The analysis has shown that increasing the etching time and applied voltage for both silver and copper solid microneedles will give less tip diameter or sharper tip. Also, if the applied voltage remains constant and etching time is increasing, then tip diameter decreases. The same is the case if the etching time remains constant and the applied voltage is increasing; then tip diameter also decreases. The effect on cone length of microneedle when the applied voltage remains constant and etching time increases is also shown in Figure 29.

Here, in this graph, the microneedle cone length effect has been measured by fixing the applied voltage and increasing the etching time. The cone length of the microneedle will be a maximum of 500 μm by bar comparison method.

After studying the literature review in detail, the comparison between the methods and techniques used by other researchers and the method and materials used in this research paper are given in Table 4.

Thus, from this comparison table, it has been found that silver and copper materials are more appropriate to use than other metals, silicon, and polymers. As they have been used in many medical treatments and even in medicines for many years, silver and copper nanoparticles are considered one of the most dynamic and fascinating nanomaterials among several metallic nanoparticles involved in biomedical applications. They are not only biocompatible but also bioinert. They are used as antibiotic agents in different biomedical applications.

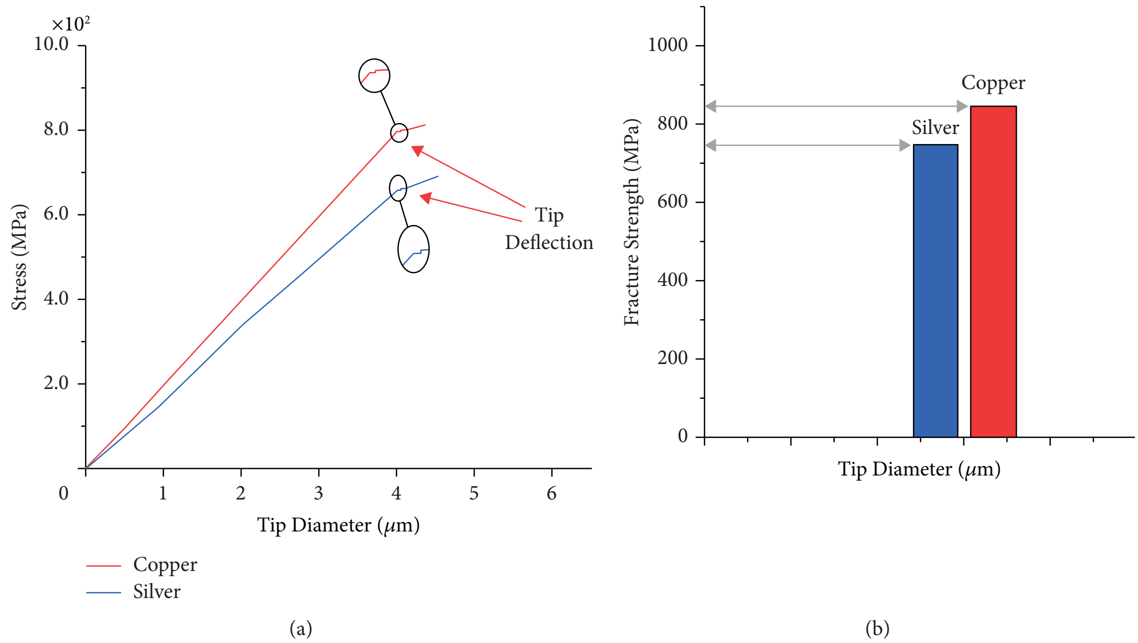


Figure 26: Graphical analysis of simulation results of deflection for both silver and copper microneedles. (a) Tip deflection comparison when stress is applied on both microneedles. (b) Fracture strength comparison based on the observed results of deflection.

Table 3: Comparison between properties of silver and copper.

Element	Silver	Copper
Ultimate tensile strength	110 MPa	210 MPa
Young's modulus of elasticity	83 GPa	120 GPa
Elastic limit	300 MPa	330 MPa
Endurance limit	40 MPa	70 MPa
Hardness	250 MPa	400 MPa

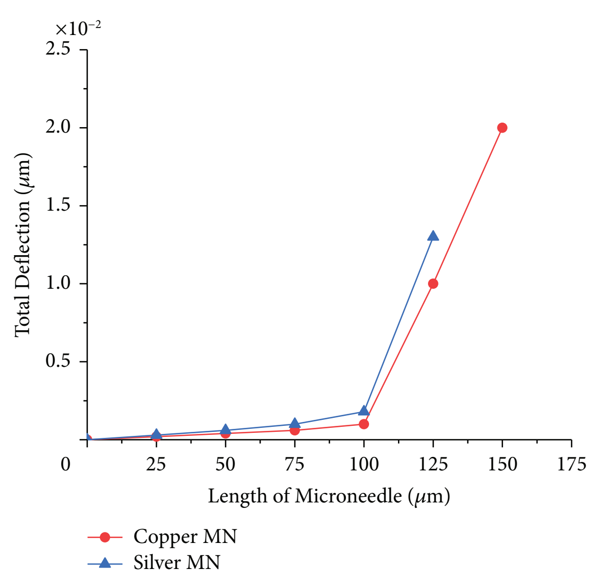


Figure 27: Structural analysis of total deflection along the length of silver and copper microneedles.

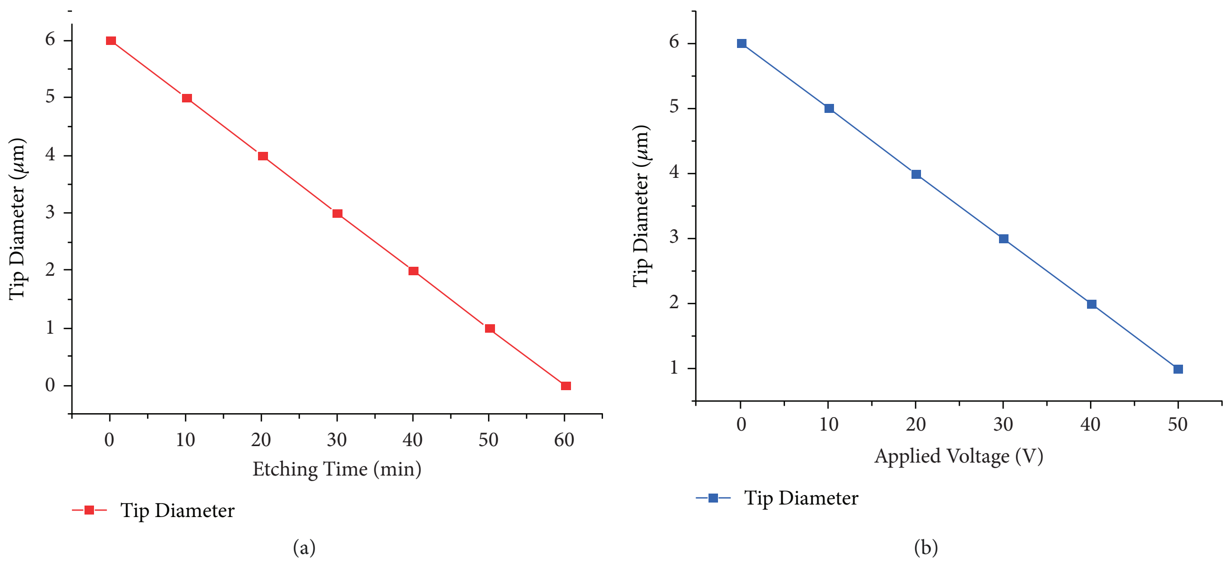


FIGURE 28: The graphs of (a) tip diameter versus etching time and (b) tip diameter versus applied voltage.

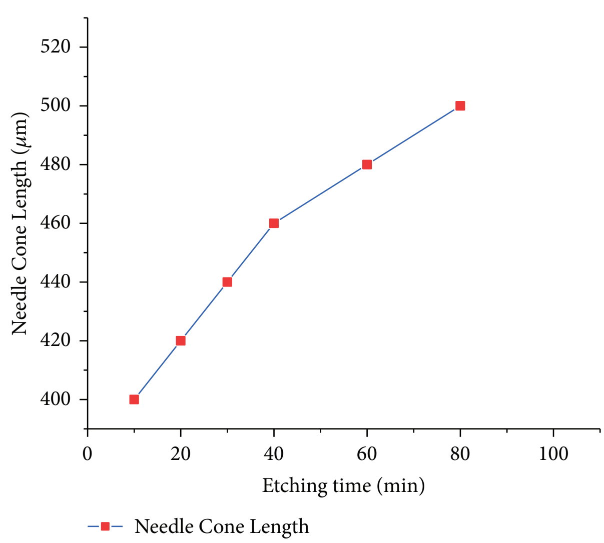


FIGURE 29: The graph of etching time versus cone length.

TABLE 4: Comparison between materials and techniques used in other works and our work.

Materials	Fabrication techniques	Advantages	Disadvantages	References
Silicon	The deep reactive ion etching process	Excellent biocompatibility and, specifically, mechanical properties are superior to polymers and metals. Also, they have nonductile nature. This technique gives much better resolution and higher aspect ratios.	Silicon microneedles are brittle and might break in insertion into the skin. This technique gives slow etch rates, low choosiness, and channel effects caused by imitated ions	[77, 78]
Stainless steel	Wet-etching photolithography	Stainless steel is characteristically more disinfected and lasts long. Wet-etching photolithography has almost no harm due to its virtuously chemical nature and is highly selective.	Stainless steel has low heat conductivity and can burn skin when heated up. Wet-etching photolithography has temperature sensitivity, poor element control, and high chemical clearance costs.	[79–82]

Table 4: Continued.

Materials	Fabrication techniques	Advantages	Disadvantages	References
Polymers	Micromolding technique	Polymers are biocompatible, biodegradable, and water-soluble. Micromolding technique is highly used for microsized objects.	The strength to size ratio of polymer is fewer as compared to metals. Cannot be machined easily and restricted speed is required for machining it. Micromolding technique is of high cost.	[83, 84]
Titanium	Surface micromachining technique or multilayer technique	Titanium is comparatively more durable and biocompatible as compared to silicon. This surface micromachining technique is more robust and reliable.	Titanium is of higher cost than other metals used and is not suitable for mass production. This technique is also of high cost.	[85–87]
Nickel	Electroless plating	Nickel is a corrosion-free and hygienic material and easily recyclable. This technique gives even coating gif nickel and smooth surface microneedles.	Some allergic reaction occurs using nickel material. High-cost technique and suitable only when the coating is involved.	[88, 89]
Silver and copper	Electrochemical etching (the electrochemical etching technique is a low-cost, clean-room-free technique and highly suitable for mass production, and no costly molding or photoresist mask is needed; it is an easily and safely used technique)	Silver is powerful, highly biocompatible, and natural antibiotic material. Silver nanoparticles are highly used in medicines for different treatments. It has ductile nature. Copper material is a biocompatible metal and endogenously exists in the human body. Copper nanoparticles have been used extensively in many medical treatments.	Silver and copper are not toxic materials so they have only minimal risk of infections and can be safely used.	Current study

Also, electrochemical etching is a low-cost technique that helps in high productivity or mass production.

8. Conclusion

To fabricate microneedles, there is a need to choose the most appropriate materials for microneedle manufacture depending on the following conditions:

(i) Manufacturing should be gentle without damaging penetrating and uneven molecules; drug release must be precise or immediate.

(ii) Mechanical strength must be sufficient for skin penetration.

Not only materials but also the appropriate technique is needed for the fabrication of solid microneedles. Many different techniques as given in Table 1 have been used. But as they are costly, and it is not economically appropriate to use them for mass production. In this research paper, numerical analysis and structural simulation have also been performed to demonstrate the deflection of the microneedles' tips and the effect of input parameters such as time and voltage on tip diameter and cone length. An economical technique for the fabrication of solid microneedle has been presented. It only costs a little as compared to other techniques for fabrication. It is easily affordable by many pharmaceutical companies. By using this technique microneedles fabrication can be increased to double at a low cost. Also, underdeveloped countries can afford this technique easily and bring microneedles technology to them as well. Not only economical techniques but also novel materials have also been chosen for the fabrication of microneedles. Silver and copper have not been used until now as a material for the fabrication of microneedle. However, they have been used for the fabrication of nanoparticles because both silver and copper are bioactive materials and have continuously been used as antibacterial coatings in many drugs or implants. This research work aims to introduce an economical and novel method for the fabrication of solid microneedles.

Data Availability

All the data and steps are given in the manuscript, and more details can be provided on demand.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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