

PHARMACEUTICAL SCIENCES FABRICATION AND TESTING OF THE NOVEL ARDUINO BASED BIO-ADHESIVITY TEST APPARATUS DESIGNED FOR TRANSDERMAL PRODUCTS

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ABSTRACT

Objective: The aim of this study is to design an apparatus for measuring the bio-adhesivity of adhesive pharmaceutical formulations.

Materials and Methods: The study utilized an Arduino Uno based microcontroller, a 40 Kg stress sensor, customized steel chassis, Natural gums and Dura Tak grade adhesives. Adhesion capacity of the adhesives was evaluated using a developed apparatus, comparing it to the manual force needed to overcome the adhesivity.^[1] Variables including the force and the amount of work the adhesives do record by the microcontroller were key focuses of the research. **Results:** The force required for detachment varied between sodium alginate (2.5 kg) and DURA TAK 87-235 2.5% solution. Adhesion strength in pressure-sensitive adhesives is influenced by cross-linking and tack force.^[2] The maximum standard deviation in the study ± 1.67 was experienced with Sodium alginate 50% solution while less standard deviation ± 0.56 with

Dura TaK-87-6908-2.5 % solution. The highest variation in the case of Sodium Alginate was attributed to its swelling index and sensitivity towards the temperature. **Conclusion:** The results obtained using the developed apparatus were reliable, demonstrating that the

instrument is cost-effective and user-friendly in a laboratory setting.

KEYWORDS: Bio-adhesivity, Adhesive formulations, Arduino Uno, Stress sensor, Sodium alginate, Dura Tak, Pressure-sensitive adhesives, Adhesion strength, Laboratory apparatus.

INTRODUCTION

Bioadhesion biological systems have the potential to be categorized into three types: Type 1 is when two biological components adhere to one another, like healing of wounds and platelet aggregation.^[3] Adhesion of a biological component to an artificial substrate is referred to as type 2 for instance, cells adhering to the development of biofilms on prosthetic devices or culture dishes. Type 3 concerns the attachment of an artificial substance to a biological substrate, such as artificial hydrogels adhering to soft tissues.^[4] Furthermore, bio adhesion is also utilized in surgical and dental applications through the use of bioadhesive materials. The study of bioadhesion has contributed to the creation of novel treatments, biomaterials, and technology goods like biosensors.^[5] The bonding between adhesive polymers and biological surfaces is typically achieved through interpenetration and subsequent non-covalent secondary bonding. Research has demonstrated that hydrogen bonding is the main mechanism of secondary bonding. Hydrophilic functional groups such as hydroxyl (-OH), sulphate (-SO₄ H), carboxyl (-COOH), and amino groups (-NH₂) are used in the creation of bio adhesive polymers.^[6] Which are advantageous for efficient target delivery. In bioadhesion, the mechanistic method is dependent on the polymer's physio-chemical characteristics.^[7] There are three key steps in the mucoadhesive process: wetting and swelling of the polymer to establish contact with the tissue, interpenetration of polymer and mucin chains, and the formation of weak chemical bonds. Polymeric hydrogels are particularly effective in exhibiting mucoadhesive properties.^[8] Some characteristics of hydrogels that contribute to their promising nature include the presence of chemical groups that form hydrogen bonds, such as carboxyl and hydroxyl groups, high molecular weight polymers, high chain flexibility polymers, and anionic surface charge, Because of these properties, hydrogels can adhere to the mucous layer. The present study focusses on the development of the apparatus with electronic arrangements.

MATERIALS AND METHODS

Load Cell stress sensor analytical grade 20Kg capacity, Amplifier module HX711, Synchronous motor AC supply 40 kg/cm² torque were mounted on the steel chasis. Arduino uno (German Make) based microcontroller was used for interfacing the system with

computer. HFX library codes were used for the programming of Arduino system. The laboratory materials used in this study included sodium alginate and Acacia purchased from CDH drug house New Delhi, CMC Sodium and HPMC 100cps procured from QualiChem's Ltd., and Dura TaK-87-6908, Dura Tak 87-2074, and Dura Tak 87-235A graciously provided as gift samples by Henkel Corporation USA.^[9] The instrument was tared before use, and the test material was applied to the plate surface with the substrate affixed. The motor was then started, and the force required for plate detachment was measured. The table presents the force required for plate detachment at different concentrations of the test adhesive.^[10]

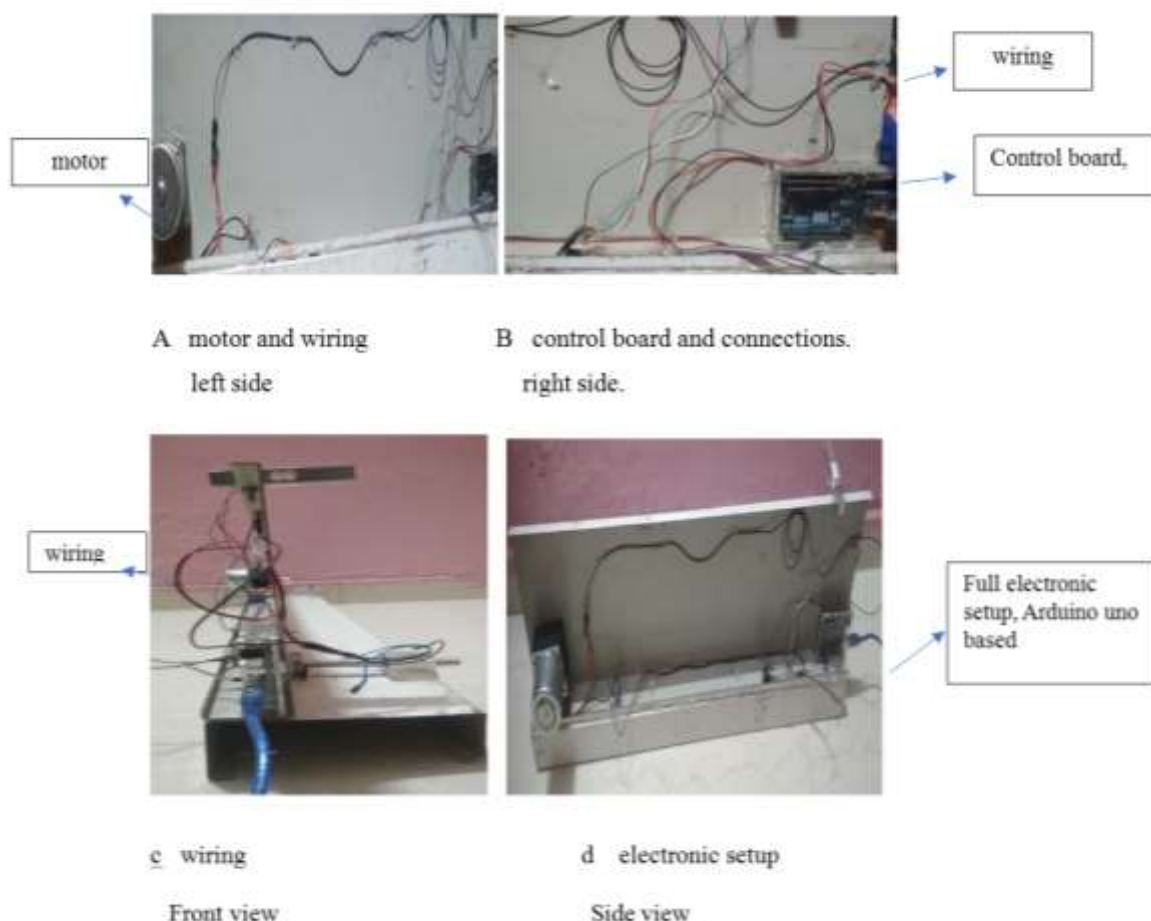


Figure: a, b, c and d 'Bio adhesion test apparatus with electronic arrangement'.^[11]

RESULTS AND DISCUSSION

Different concentration of the adhesive materials was applied on the glass plate and then force for detachment was measured with the developed apparatus. The results are given here as under:

Table 1: Bio-adhesion strength measurement on apparatus developed.

S.No	Test Material	Force recorded for d ^[12] etachment in kg over force transducer	Refference
1	Sodium alginate 50% w/v	2.5 ± 0.87	[12]
2	Acacia 40% w/v	2.7 ± 0.67	[13]
3	CMC 4% w/v	3.5 ± 0.88	[14]
4	SodiumAlginate,50%(0,10)w/v	3.8 ± 1.67	[11]
5	HPMC 20% w/v	4.3 ± 0.78	[15]
6	HPMC 30% w/v	4.8 ± 0.80	[16]
7	Dura TaK-87-6908-2.5 % w/v	5.9 ± 0.56	[17]
8	Dura Tak 87- 2074-2.5 % w/v	6.2 ± 1.65	[18]
9	Dura Tak 87- 235A-2.5% w/v	7.5 ± 0.79	[18]

Note: The table shows the mean force recorded for detachment with the associated standard deviation. Based on measurements taken using the developed apparatus.^[19]

The least force was measured with the solution of sodium alginate requiring about 2.5 kg of the force for the total detachment of the plate. And highest force was required with DURA TAK 87-235 2.5% solution i.e. 7.5 ± 0.79 Kg.^[20] There are three primary categories in which a polymer and the mucous layer interact: covalent chemical bonds, secondary chemical bonds, and mechanical or physical bonds.^[21] Physical linkages occur when mucin glycoproteins become entangled with the polymer chains, allowing the mucin chains to interpenetrate the matrix of polymers. The extent of this interpenetration depends on the flexibility of the macromolecules' chains and their diffusion coefficients.^[22] Secondary chemical bonds encompass interactions such as van der Waals forces and hydrogen bonding. Polymers like Acacia, HPMC and Sodium CMC possesses surface charges on them. Hence interaction of the polymer chain with the mucin structure is important for the adhesion.^{[21],[22]} Hydrogen bonding plays a crucial role in mucoadhesion as it creates a connection, between the mucoadhesive polymer and the functional groups. Hydrogen bond formation involves functional groups including hydroxyls, carboxyl's, sulphates, and amino groups which contributes to the establishment of good mucoadhesive properties.^[23] The charge contained in the polymer structure and wetting of target surface play important factors in achieving good bioadhesion.^[24] Additionally, spreading over a larger area enhances the interaction and adhesion between the polymers and the surface. Comparatively, the HPMC and Duratak solutions demonstrate higher adhesion than the more viscous solutions of Sodium alginate (50% w/v), Acacia (40% w/v), and Sodium Alginate (50% w/v). Among the Dura Tak grades used the least adhesion was observed with DuraTak 87-6908 i.e. 5.9 ± 0.56 and highest adhesion was observed with the Dura Tak 87-235A (2.5% solution).^[19] The force recorded

with Duratak 87-235A was 7.5 ± 0.79 which is more than Dura Tak 87- 2074 i.e 6.2 ± 1.65 Kg. The difference between the force of adhesion between various grades is attributed to the chemical nature of Dura tak Adhesives.^[25] The measurements made with the instruments were repeated three time. The standard deviation minimum variation in the measurement was 0.56Kg and maximum variation was 1.67 Kg.

Preparation of Adhesive Formulations: The adhesive formulations were prepared by first selecting and purifying natural gums. These gums were dissolved in distilled water, filtered to remove impurities, and then dried. The purified gums were then blended with Dura Tak grade adhesives in varying proportions, ensuring uniform distribution using a mechanical stirrer.^[26] The blended mixtures were spread into thin layers and dried at controlled temperatures to form consistent adhesive films, which were then cut into uniform samples for testing. Detailed records of the formulation composition, including the proportions of natural gums and Dura Tak adhesives, as well as processing conditions such as times, temperatures, and equipment used, were maintained to ensure consistency and reproducibility in the testing of their bio-adhesivity.

Mechanism and Working: The apparatus work by applying a controlled force to the adhesive sample until the bond is broken, with the stress sensor measuring the force required up to 40 kg. The Arduino Uno records the force and calculates the work done by the adhesive. Natural gums and Dura Tak grade adhesives were tested, with data analysed to determine the adhesion strength. The stress sensor is connected to a movable arm or platform that applies force to the adhesive sample. As the arm moves, the force applied is gradually increased until the adhesive bond is broken. The system ensures accurate, precise, and consistent measurements, providing a reliable method for comparing different adhesive formulations and improving the evaluation process over manual methods.

Conclusion: Bioadhesion is a significant phenomenon in biological systems, with various applications in medicine and technology. It can be categorized into three types based on the nature of adhesion Type 1 is when two biological components adhere to one another, like healing of wounds and platelet aggregation.^[27] Adhesion of a biological component to an artificial substrate is referred to as type 2 for instance, cells adhering to the development of biofilms on prosthetic devices or culture dishes. Type 3 concerns the attachment of an artificial substance to a biological substrate, such as artificial hydrogels adhering to soft tissues.^[28] Type 1 involves adhesion between two biological components, such as platelet

aggregation and wound healing. Type 2 refers to the adhesion of a biological component to an artificial substrate, like cells adhering to culture dishes or the formation of biofilms on prosthetic devices.^[29] Type 3 pertains to the adhesion of an artificial material to a biological substrate, for example, synthetic hydrogels adhering to soft tissues.

The study of bioadhesion has contributed in the creation of novel treatments, biomaterials, and technology goods like biosensors.^[30] Adhesive polymers and biological surfaces bind together by interpenetration and subsequent secondary non-covalent bonding. Research has shown that hydrogen bonding is the primary mechanism of secondary bonding in bioadhesion.^[17] Bioadhesive polymers are designed with hydrophilic functional groups, including amino groups (-NH₂), hydroxyl (-OH), sulphate (-SO₄ H), and carboxyl (-COOH), which facilitate efficient target delivery.^{[19],[31]}

The mechanistic approach to bioadhesion depends on the physico-chemical properties of the polymer used.^[16] The process of mucoadhesion, in particular, involves three key steps. First, the polymer undergoes wetting and swelling to establish contact with the tissue. Second, there is interpenetration of polymer and mucin chains. Finally, weak chemical bonds are formed between the polymer and the mucous layer.^{[15],[27]}

Polymeric hydrogels are known for their excellent mucoadhesive properties.^[32] They possess characteristics like the existence of chemical groups that form hydrogen bonds (such as carboxyl's and hydroxyls), an anionic surface charge, a high molecular weight polymer, and a high degree of chain flexibility.^[33]

These properties enable hydrogels to spread onto the mucus layer, enhancing their interaction and adhesion with the surface.^[34]

In our study, we focused on the development of an apparatus with electronic arrangements to measure the bio-adhesion strength.^{[35],[36]} The apparatus consisted of a load cell stress sensor, an amplifier module, and a synchronous motor. We used an Arduino-based microcontroller for system interfacing. Various adhesive materials, including sodium alginate, Acacia, CMC, HPMC, and different grades of Dura Tak, were tested using the apparatus.^{[37], [38]} The force required for plate detachment was measured, and the results were recorded.

We observed that the least force was required for the detachment of the plate when using sodium alginate, while the highest force was needed for Dura Tak 87-23 5A.^{[39][11]} The

interactions between the adhesive materials and mucous layer include covalent chemical bonds, secondary chemical bonds (such as van der Waals forces and hydrogen bonds), and physical or mechanical linking.^[26]

The presence of surface charges on polymers like Acacia, HPMC, and Sodium CMC is important for the interaction and adhesion between the polymer chain and the mucin structure.^[13]

Hydrogen bonding, facilitated by functional groups like amino groups, sulphates, carboxyl's, and hydroxyls, plays a crucial role in achieving good mucoadhesive properties. Additionally, the charge present in the polymer structure and the wetting of the target surface significantly contribute to successful bioadhesion.^{[37],[40]} Moreover, the spreading of adhesive materials over a larger area enhances their interaction and adhesion with the surface.^[12]

Comparatively, HPMC and Duratak solutions demonstrated higher adhesion compared to more viscous solutions of sodium alginate and Acacia. Among the various grades of Dura Tak, we observed that Dura Tak 87-235A exhibited the highest adhesion, while Dura Tak 87-6908 showed the least adhesion.^[41]

The force measurements were repeated three times, and the standard deviation indicated minimal variation in the measurements.^[42]

In conclusion, the study of bioadhesion and mucoadhesion offers significant insights into the development of new therapies and biomaterials. Understanding the physio-chemical properties of adhesive polymers and their interactions with biological surfaces can lead to the design of more efficient bio-adhesive materials. The apparatus with electronic arrangements used in our study provided valuable data on the adhesive strength of various materials.^[43] Further research in this field will contribute to advancements in medicine, dentistry, and other related applications.

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REFERENCE

1. L. Vaut, E. Scarano, G. Tosello, and A. Boisen, *Fully replicable and automated retention measurement setup for characterization of bio-adhesion*, 2019; 6. The Authors, doi: 10.1016/j.ohx.2019.e00071.
2. S. Awwad *et al.*, "Principles of pharmacology in the eye," *Br. J. Pharmacol.*, Dec. 2017; 174(23): 4205–4223, doi: 10.1111/BPH.14024.
3. W. Duan, X. Bian, and Y. Bu, "Applications of Bioadhesives: A Mini Review," *Front. Bioeng. Biotechnol.*, vol. 9, no. September, 2021; 1–12, doi: 10.3389/fbioe.2021.716035.
4. A. Assmann *et al.*, "A highly adhesive and naturally derived sealant," *Biomaterials*, 2017; 140: 115–127, doi: 10.1016/j.biomaterials.2017.06.004.
5. Y. C. Cheng, T. S. Li, H. L. Su, P. C. Lee, and H. M. D. Wang, "Transdermal delivery systems of natural products applied to skin therapy and care," *Molecules*, 2020; 25(21): 1–21, doi: 10.3390/molecules25215051.
6. B. Sharmila *et al.*, "Modelling and performance analysis of electric vehicle," *Int. J. Ambient Energy*, 2022; 43(1): 5034–5040, doi: 10.1080/01430750.2021.1932587.
7. G. Cattelan *et al.*, "Alginate Formulations: Current Developments in the Race for Hydrogel-Based Cardiac Regeneration," *Front. Bioeng. Biotechnol.*, May, 2020; 8, doi: 10.3389/fbioe.2020.00414.
8. B. Devarshi, "Bioadhesive drug delivery systems: overview and recent advances Devarshi Brahmabhatt," *Int. J. Chem. Life Sci.*, 2017; 6.33(2017): 2016–2024.
9. J. W. Lee, J. H. Park, and J. R. Robinson, "Bioadhesive-based dosage forms: The next generation," *J. Pharm. Sci.*, 2000; 89(7): 850–866, doi: 10.1002/1520-6017(200007)89:7<850::aid-jps2>3.3.co;2-7.
10. E. Perez and F. Pincet, "Bioadhesion," *Peyresq Lect. Nonlinear Phenom.*, 2012; 3(2): 241–278, doi: 10.1142/9789814440592_0006.
11. J. Deng *et al.*, "Electrical bioadhesive interface for bioelectronics," *Nat. Mater.*, 2021; 20(2): 229–236, doi: 10.1038/s41563-020-00814-2.
12. A. Dey, P. Bhattacharya, and S. Neogi, "Bioadhesives in biomedical applications: A critical review," *Rev. Adhes. Adhes.*, 2020; 8(2): 130–152, doi: 10.7569/RAA.2020.097308.
13. Y. Bu and A. Pandit, "Cohesion mechanisms for bioadhesives," *Bioact. Mater.*, November 2021; 13: 105–118, 2022, doi: 10.1016/j.bioactmat.2021.11.008.
14. F. Cilurzo, C. G. M. Gennari, and P. Minghetti, "Adhesive properties: A critical issue in transdermal patch development," *Expert Opin. Drug Deliv.*, 2012; 9(1): 33–45, doi:

- 10.1517/17425247.2012.637107.
15. D. E. Chickering, J. S. Jacob, and E. Mathiowitz, "Bioadhesive microspheres, II. Characterization and evaluation of bioadhesion involving hard, bioerodible polymers and soft tissue," *React. Polym.*, 1995; 25(2–3): 189–206, doi: 10.1016/0923-1137(94)00098-P.
16. K. Kumar, N. Dhawan, H. Sharma, S. Vaidya, and B. Vaidya, "Bioadhesive polymers: Novel tool for drug delivery," *Artif. Cells, Nanomedicine Biotechnol.*, 2014; 42(4): 274–283, doi: 10.3109/21691401.2013.815194.
17. J. Wunderer *et al.*, "A mechanism for temporary bioadhesion," *Proc. Natl. Acad. Sci. U. S. A.*, 2019; 116(10): 4297–4306, doi: 10.1073/pnas.1814230116.
18. F. Nihal Tüzün and M. Safak Tunalioğlu, "The effect of finely-divided fillers on the adhesion strengths of epoxy-based adhesives," *Compos. Struct.*, 2015; 121: 296–303, doi: 10.1016/j.compstruct.2014.11.007.
19. L. Kumar, S. Verma, B. Vaidya, and V. Gupta, *Bioadhesive Polymers for Targeted Drug Delivery*. Elsevier Inc., 2017. doi: 10.1016/B978-0-12-809717-5.00012-9.
20. M. L. B. Palacio and B. Bhushan, "Research article: Bioadhesion: A review of concepts and applications," *Philos. Trans. R. Soc. A Math. Phys. Eng. Sci.*, 2012; 370(1967): 2321–2347, doi: 10.1098/rsta.2011.0483.
21. K. M. Tur and H. S. Ch'ng, "Evaluation of possible mechanism(s) of bioadhesion," *Int. J. Pharm.*, 1998; 160(1): 61–74, doi: 10.1016/S0378-5173(97)00297-4.
22. P. Kingshott and H. J. Griesser, "Surfaces that resist bioadhesion," *Curr. Opin. Solid State Mater. Sci.*, 1999; 4(4): 403–412, doi: 10.1016/S1359-0286(99)00018-2.
23. S. Nam and D. Mooney, "Polymeric Tissue Adhesives," *Chem. Rev.*, 2021; 121(18): 11336–11384, doi: 10.1021/acs.chemrev.0c00798.
24. N. A. Peppas and P. A. Buri, "Surface, interfacial and molecular aspects of polymer bioadhesion on soft tissues," *J. Control. Release*, 1985; 2(C): 257–275, doi: 10.1016/0168-3659(85)90050-1.
25. D. Khan, M. Qindeel, N. Ahmed, A. U. Khan, S. Khan, and A. U. Rehman, "Development of novel pH-sensitive nanoparticle-based transdermal patch for management of rheumatoid arthritis," <https://doi.org/10.2217/nnm-2019-0385>, Feb. 2020; 15(6): 603–624, doi: 10.2217/NNM-2019-0385.
26. S. Asati, S. Jain, and A. Choubey, "Bioadhesive or Mucoadhesive Drug Delivery System: A Potential Alternative to Conventional Therapy," *J. Drug Deliv. Ther.*, 2019; (9A): 858–867, [Online]. Available: <http://jddtonline.info>

27. J. K. Vasir, K. Tambwekar, and S. Garg, "Bioadhesive microspheres as a controlled drug delivery system," *Int. J. Pharm.*, 2003; 255(1–2): 13–32, doi: 10.1016/S0378-5173(03)00087-5.
28. Y. Xiong *et al.*, "A review of the properties and applications of bioadhesive hydrogels," *Polym. Chem.*, 2021; 12(26): 3721–3739, doi: 10.1039/d1py00282a.
29. C. Kang and S. C. Shin, "Preparation and evaluation of bioadhesive dibucaine gels for enhanced local anesthetic action," *Arch. Pharm. Res.*, 2010; 33(8): 1277–1283, doi: 10.1007/s12272-010-0819-8.
30. E. Freundlich, N. Shimony, A. Gross, and B. Mizrahi, "Bioadhesive microneedle patches for tissue sealing," *Bioeng. Transl. Med.*, 2024; 9(3): 1–10, doi: 10.1002/btm2.10578.
31. M. L. B. Palacio, S. R. Schricker, and B. Bhushan, "Bioadhesion of various proteins on random, diblock and triblock copolymer surfaces and the effect of pH conditions," *J. R. Soc. Interface*, 2011; 8(58): 630–640, doi: 10.1098/rsif.2010.0557.
32. X. Pei, J. Wang, Y. Cong, and J. Fu, "Recent progress in polymer hydrogel bioadhesives," *J. Polym. Sci.*, 2021; 59(13): 1312–1337, doi: 10.1002/pol.20210249.
33. N. A. Peppas and J. J. Sahlin, "Hydrogels as mucoadhesive and bioadhesive materials: A review," *Biomaterials*, 1996; 17(16): 1553–1561, doi: 10.1016/0142-9612(95)00307-X.
34. H. Chopra, S. Kumar, and I. Singh, "Bioadhesive Hydrogels and Their Applications," *Bioadhesives Drug Deliv.*, 2020; 147–170, doi: 10.1002/9781119640240.ch6.
35. K. Peh, T. Khan, and H. Ch'ng, "Mechanical, bioadhesive strength and biological evaluations of chitosan films for wound dressing," *J. Pharm. Pharm. Sci.*, 2000; 3(3): 303–311.
36. G. Shinde, S. Sudharshini, B. Stephenrathinaraj, C. H. Rajveer, D. Kumaraswamy, and G. S. Bangale, "Formulation and evaluation of mucoadhesive tablets of niacin using different bioadhesive polymers," *Int. J. Pharma Bio Sci.*, 2010; 1(2).
37. R. E. Baier, A. E. Meyer, J. R. Natiella, R. R. Natiella, and J. M. Carter, "Surface properties determine bioadhesive outcomes: Methods and results," *J. Biomed. Mater. Res.*, 1984; 18(4): 337–355, doi: 10.1002/jbm.820180404.
38. H. Ueda, M. Mutoh, T. Seki, D. Kobayashi, and Y. Morimoto, "Acoustic cavitation as an enhancing mechanism of low-frequency sonophoresis for transdermal drug delivery," *Biol. Pharm. Bull.*, 2009; 32(5): 916–920, doi: 10.1248/bpb.32.916.
39. C. S. Li, L. Chen, D. Chen, and S. Wang, "Formulation and development of bioadhesive transdermal gel of ropivacaine loaded nanoparticles for enhancement of anesthetic effect: Preclinical study in animal model," *Pak. J. Pharm. Sci.*, 2023; 36(3): 843–848, doi:

- 10.36721/PJPS.2023.36.3.REG.843-848.1.
40. K. L. Mittal, I. S. Bakshi, and J. K. Narang, "Part 1 FUNDAMENTAL ASPECTS 3," 2020.
41. A. Kinloch, "Introduction to adhesion and adhesives," *Eur. Struct. Integr. Soc.*, 2001; 28(C): 199–202, doi: 10.1016/S1566-1369(01)80034-0.
42. I. Singh and P. Paramjot, *Bioadhesives in drug delivery*, 2017. doi: 10.1201/9781315120942.
43. G. C. Miceli, A. Martorana, F. Cancilla, G. Pitarresi, M. Licciardi, and F. S. Palumbo, "Synthesis, Characterization, and Processing of Highly Bioadhesive Polyurethane Urea as a Microfibrous Scaffold Inspired by Mussels," *ACS Appl. Polym. Mater.*, 2023; 5(10): 8483–8494, doi: 10.1021/acsapm.3c01578.