

An overview of different variety of needle-skinned animals



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Abstract

Artificial skin models have drawn interest as an alternative to animal testing for determining the safety and toxicity of items since 2013, since ethics for animal experimentation have been reinforced in the European Union. Different artificial skin models have been created by mixing various biomaterials and human cells as well as employing a number of processes, including freeze-drying, 3-D printing, electro spinning, and microfluidic system, driven by regulatory authorities and industrial needs. For the evaluation of safety and efficacy in the cosmetic and pharmaceutical industries as well as for the fundamental studies on cell to cell interactions, cell to extracellular matrix interactions, tissue formation and development, intricately designed artificial skin models that closely resemble human skin can be highly valuable and effective tools. This article summarizes several manufacturing methods for synthetic skin models and their primary uses.

Keywords: Artificial skin models, Animal alternatives, Safety evaluation, Toxicity, Animal-free testing.

Introduction

In the UK, there are more than 10,000 pig farms, and in 2020, more than 8.9 million pigs were raised for slaughter. 60% of the UK industry is made up of indoor pig production. In the first few days after birth, it is customary to inject piglets with 200 mg of iron dextran into the ham or neck muscle. Iron deficiency anaemia, which may slow growth rates, make people more susceptible to illness, and increase mortality, is prevented by parenteral iron supplementation. Multiple post-natum injections may be necessary, especially on organic farms where piglets undergo prolonged nursing periods, since one dose of iron may not be sufficient for optimum development.

In cattle husbandry, using the same needles on different animals is commonplace. For instance, only 6% (n = 4) of responders to a UK study on cow vaccination methods reported using a fresh needle for each animal. Additionally, according to a poll of 360 sheep producers, 3.3% always replaced their needles after each animal, 20.3% after 15-20 doses, 32.4% after 50 doses, 39.5% after 100 doses, and 4.5% chose the "other" option.

Contrary to recommendations from the Agriculture and Horticulture Development Board (AHDB), which asserts that needles are designed to be used only once and should, at the very least, be changed every ten animals when injecting a large number of animals, is the practise of repeatedly using needles until they become blunt. In order to lower the danger of broken needles contaminating meat products and injection site lesions, food assurance programmes like Red Tractor advise regular needle swaps. Resources on iron injection provide contradictory suggestions, such as suggesting a new needle for each piglet or every litter. Due to its efficiency and simplicity, automated self-filling syringes are extensively employed in intensive pig farms. It is possible to fit specialised needles with an adapter that sterilises them between injections. However, it is advised to replace the needle every 100 shots, which gives the needle a chance to dull. If needles are shared among animals, reuse might raise the risk of infection spreading. Following intramuscular delivery of a *Mycoplasma* vaccine, research reported the needle-transmission of swine reproductive and respiratory disease virus to susceptible pigs. Bluetongue virus spread from infected to uninfected ruminants when the same needle was used to inject phosphate-buffered saline subcutaneously. Injection or oral iron dose produced identical behavioural and cortisol responses to sham-treated pigs, according to one research that looked at the welfare effects of the iron delivery strategy in piglets. In humans, insertion pain frequency increased with needle diameter and, in healthy volunteers, rose in direct proportion to the force needed to penetrate the skin. Others have shown that after a puncture, a needle's tip deforms and tissue products stick to the harmed metal, which might result in further tissue trauma and discomfort if the needle is used again.

Repeated usage may cause needles to distort, making them more likely to break. Sharp or crooked needles might exacerbate tissue injury and result in carcass flaws. According to one research in sows, lesion prevalence at injection sites in the neck and hip was 11.2% and 2.7%, respectively. Additionally, it has been calculated that during a 3-month period, the incidence of head and neck abscesses in pigs at slaughter was 2.51%. In contrast to zero recorded losses when needle-free methods are employed, the annual number of pigs put to death because of broken needles that cannot be collected has been calculated at 1.23 per year per 1200-sow barn.

Pain Management

A noxious stimulus is converted into electrical impulses in the peripheral terminals of nociceptor sensory fibres during transduction, which is the initial stage of nociception. Nociceptors, or free ends of first-order afferent neurons (A and C fibres) in the pain pathway, are basically sensory receptors. Mechanical and heat stimuli activate the bigger, swifter-conducting weakly myelinated A fibres, which provide the first, acute pain experienced at the site of the lesion. On the other hand, the activation threshold of the smaller, slower-conducting unmyelinated C fibres is high and they react to chemical, mechanical, and thermal stimuli. As a result, these fibres are linked to a more enduring, diffused pain. These nociceptors pick up noxious stimuli and convert them into electric signals that are subsequently sent to the CNS. The dorsal root ganglion houses the cell bodies of both the A and C fibres, enabling quick transmission of the signal from the periphery to the spinal cord.

The process of conduction of action potentials from the peripheral terminal through axons to the central terminal of nociceptors in the central nervous system is known as transmission and comes after transduction. First-order neurons go from the skin's stimulation site to the spinal cord through the dorsal root, where they connect with second-order neurons in the dorsal horn to convey the noxious information. The C fibres terminate in lamina II of the dorsal horn, whereas the A fibres do so in laminae I and V (referred to as Rexed laminae). Before rising to the brain, these second-order neurons then switch sides of the spinal cord. The spinothalamic and spinoreticular tracts, which are found in the anterolateral white matter of the spinal cord, are the two principal channels that convey nociceptive signals from the spinal cord to the brain. Second-order neurons in the first route climb from the contralateral spinothalamic tract before coming to an end in the ventral posterolateral and central nuclei of the thalamus, where they create synapses with third-order neurons that are crucial for processing somatosensory data. The ipsilateral post-central gyrus (primary somatosensory cortex) is where the third-order neuron terminates after projecting through the posterior limb of the internal capsule; this route is crucial in the location and intensity of the painful stimuli. The spinoreticular tract, which is responsible for the emotional component of pain, simultaneously ascends the contralateral cord to the brainstem's reticular formation before

continuing up to the thalamus, hypothalamus, and finally the cortex. As a result, the cortex will receive pain signals from the skin and interpret them as pain. The third nociception step is the sense of pain.

Conclusion

In both fundamental and practical research, it is crucial to understand the healthy and sick states of skin. Animal models are often employed in fundamental research to understand the healthy and pathological states of human skin, as well as in the preclinical stage to determine a drug's mechanism of action and assess its effectiveness. But there has always been controversy over the moral issues of using animals in research. Animal models often fail to accurately anticipate the human response owing to variations in skin physiology and immunology, in addition to the main ethical problem. Other limitations of using animal models are their expensive cost, lengthy methodology, and high level of experimental competence. The development and validation of alternatives to in vivo animal experiments has recently been tried using an advanced tissue engineering methodology combining biomaterials and skin cells. Freeze-drying, 3-D printing, electrospinning, and microfluidic systems are just a few of the methods that may be used to create 3-D artificial skin models that closely resemble human healthy or sick skin. A well-defined and stratified 3-D architecture that simulates the in vivo milieu is provided by 3-D constructions, which range from a simple one-layer skin model to a more intricate one that includes all three layers. In addition, 3-D scaffolds have recently been developed with the integration of various cell types (melanocytes, stem cells, Langerhans cells, endothelial cells, and immune cells) to simulate healthy or sick skin. The traditional approach based on collagen gel dermal matrix combined with fibroblasts and keratinocytes still serves as the gold standard in 3-D artificial skin engineering despite the development of new fabrication techniques. This is due to some problems with the tissue engineering approach that need to be resolved, such as standardisation of fabrication processes, quality control, the establishment of analytical methods, and data correlation between in vivo and in vitro. Despite these problems, we think that 3-D artificial skin models are a very useful tool for fundamental in vitro investigations of cell-cell/cell-ECM interactions, tissue

formation, and skin disease, as well as for assessing safety and effectiveness in the cosmetic and pharmaceutical sectors

References

1. Abd E, Yousef SA, Pastore MN, Telaprolu K, Mohammed YH, Namjoshi S, Grice JE, Roberts MS (2016) Skin models for the testing of transdermal drugs. *Clin Pharmacol* 8:163–176
2. Ackermann K, Borgia SL, Korting HC, Mewes KR, Schafer-Korting M (2010) The phenion full-thickness skin model for percutaneous absorption testing. *Skin Pharmacol Physiol* 23(2):105–112
3. Ahadian S, Civitarese R, Bannerman D, Mohammadi MH, Lu R, Wang E, Davenport-Huyer L, Lai B, Zhang B, Zhao Y, Mandla S, Korolj A, Radisic M (2018) Organ-On-A-Chip platforms: a convergence of advanced materials, cells, and microscale technologies. *Adv Healthc Mater* 7(2)
4. Ahn SH, Yoon H, Kim GH, Kin YY, Lee SH, Chun W (2010) Designed three-dimensional collagen scaffolds for skin tissue regeneration. *Tissue Eng C* 16(5):813–821
5. Atac B, Wagner I, Horland R, Lauster R, Marx U, Tonevitsky AG, Azar RP, Lindner G (2013) Skin and hair on-a-chip: in vitro skin models versus ex vivo tissue maintenance with dynamic perfusion. *Lab Chip* 13(18):3555–3561
6. Bernard G, Auger M, Soucy J, Pouliot R (2007) Physical characterization of the stratum corneum of an in vitro psoriatic skin model by ATR-FTIR and Raman spectroscopies. *Biochim Biophys Acta* 1770(9):1317–1323
7. Brohem CA, Cardeal LB, Tiago M, Soengas MS, Barros SB, MariaEngler SS (2011) Artificial skin in perspective: concepts and applications. *Pigment Cell Melanoma Res* 24(1):35–50
8. Cheluvappa R, Scowen P, Eri R (2017) Ethics of animal research in human disease remediation, its institutional teaching; and alternatives to animal experimentation. *Pharmacol Res Perspect* 5(4):e00332

9. Chen H, Peng Y, Wu S, Tan LP (2016) Electrospun 3D fibrous scaffolds for chronic wound repair. *Materials (Basel)* 9(4):272
10. Cubo N, Garcia M, Del Canizo JF, Velasco D, Jorcano JL (2016) 3D bioprinting of functional human skin: production and in vivo analysis. *Biofabrication* 9(1):015006
11. Do AV, Khorsand B, Geary SM, Salem AK (2015) 3D printing of scaffolds for tissue regeneration applications. *Adv Healthc Mater* 4(12):1742–1762
12. Driskell RR, Lichtenberger BM, Hoste E, Kretzschmar K, Simons BD, Charalambous M, Ferron SR, Herault Y, Pavlovic G, Ferguson-Smith AC, Watt FM (2013) Distinct fibroblast lineages determine dermal architecture in skin development and repair. *Nature* 504(7479):277–281
13. Flaten GE, Palac Z, Engesland A, Filipovic-Grcic J, Vanic Z, Skalko-Basnet N (2015) In vitro skin models as a tool in optimization of drug formulation. *Eur J Pharm Sci* 75:10–24
14. Fu L, Xie JW, Carlson MA, Reilly DA (2017) Three-dimensional nanofiber scaffolds with arrayed holes for engineering skin tissue constructs. *MRS Commun* 7(03):361–366
15. Gangatirkar P, Paquet-Fifield S, Li A, Rossi R, Kaur P (2007) Establishment of 3D organotypic cultures using human neonatal epidermal cells. *Nat Protoc* 2(1):178–186
16. Garland MJ, Migalska K, Tuan-Mahmood TM, Singh TRR, Majithija R, Caffarel-Salvador E, McCrudden CM, McCarthy HO, Woolfson AD, Donnelly RF (2012) Influence of skin model on in vitro performance of drug-loaded soluble microneedle arrays. *Int J Pharm* 434(1–2):80–89
17. Groeber F, Holeiter M, Hampel M, Hinderer S, Schenke-Layland K (2011) Skin tissue engineering—in vivo and in vitro applications. *Adv Drug Deliv Rev* 63(4–5):352–366
18. Haslik W, Kamolz LP, Nathschlager G, Andel H, Meissl G, Frey M (2007) First experiences with the collagen-elastin matrix Matriderm as a dermal substitute in severe burn injuries of the hand. *Burns* 33(3):364–368
19. Haslik W, Kamolz LP, Manna F, Hladik M, Rath T, Frey M (2010) Management of full-thickness skin defects in the hand and wrist region: first long-term experiences with the dermal matrix Matriderm. *J Plast Reconstr Aesthet Surg* 63(2):360–364

20. Hilmi AB, Halim AS, Hassan A, Lim CK, Noorsal K, Zainol I (2013) In vitro characterization of a chitosan skin regenerating template as a scaffold for cells cultivation. SpringerPlus 2(79):1–9

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