International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 02 Issue 09 September 2022

Page No: 935-940

DOI: https://doi.org/10.47191/ijmscrs/v2-i9-06, Impact Factor: 5.365

In Vitro Degradation and *In Vivo* Skin sensitisation study of Hernia Mesh - Sterilized Partially Absorbable Tissue Separating Dual Layered Surgical Mesh

Minocha Dr. Pramod Kumar[1], Kothwala Deveshkumar Mahendralal[2], Durani Mohamadovesh Mohamadyasin[3], Shaikh Aamir Sohel Mukhtar[4]

[1,2,3,,4] Meril Life Sciences Pvt. Ltd., Bilakhia House, Survey No. 135/139, Muktanand Marg, Chala, Vapi, Dist - Valsad - 396 191, Gujarat, India.

ABSTRACT

As hernia mesh implants are used to reinforce the abdominal wall, several complications can occur, such as hernia recurrence, abdominal pain, seroma formation and infection, depending on their biocompatibility. The polymer coated knitted mesh is used to repair hernias by providing a flexible scaffold. The objective of this study was to assess skin sensitisation potential of polar and non-polar extract and *In Vitro* degradation and *In Vivo* skin sensitisation pattern for polymer coated knitted mesh. The guinea pig maximization test (GPMT) is usually performed with one moderately irritant induction dose of the allergen and gives a qualitative assessment hazard identification of the allergenicity of the chemical. The apparent morphological change, weight, and strength loss rate of the mesh all showed the degrading impact. The degradation of polymer coated knitted mesh is performed to check polymer layer pattern after implantation.

KEYWORDS: Hernia Mesh, Skin sensitisation, *In Vitro*, *In Vivo*, and Degradation

ARTICLE DETAILS

Published On:
10 September 2022

Available on:
https://ijmscr.org/

INTRODUCTION

Owing to the increase recurrence prevalence of hernias, surgeons commonly use surgical mesh to fortify hernia repairs and reduce recurrence. Since the 1980s, mesh-based hernia repairs have been on the rise; non-mesh procedures accounted for less than 10 % of groin hernia treatments by 2000. Recurrent hernias can be significantly minimized when mesh made of either material like the examples of polymer include without limitation, Poly-L-lactide-co-caprolactone, poly caprolactone, poly-dl-lactic acid, poly glycerolse bacate or mixture thereof is used. Mesh, on the other hand, isn't required to close the abdominal wall gap. Some mesh therapy uses the body's own tissues, which reduces the risks connected with implants, such as host versus graft rejection. A hernia requires surgery to repair the defect; nevertheless, post-operative complications such as prolonged pain, adhesion, and infection are common. The most common adverse effects of hernia mesh include pain, infection, hernia recurrence, adhesion, and intestinal obstruction. Another possible negative effect of hernia mesh installation is migration and shrinkage (contraction). It is usual to hear success percentages ranging from 90 % to 100 %. Mesh repairs have a reduced risk of hernia recurrence than non-mesh operations in many cases. Unfortunately, certain repairs have a significant risk of chronic discomfort, ranging from 5 to 15 %. In terms of recurrence, hernias were addressed with treatments including direct suture and tissue repair. However, when used on a patient, the usual techniques were ineffective and had disastrous effects. To address the issues raised by the aforementioned treatments, the hernia repair process, a new surgical method used to treat hernias, is undertaken for in-vitro as well as *In vivo* to understand the effect of degradable coatings to assess skin sensitisation of polar and non-polar extract using polymer coated knitted mesh. A polymer preferably degradable coating of film was applied to the mesh prosthesis. The examples of polymers for film include poly-L-lactide-co-caprolactone, poly caprolactone, poly-dl-lactic acid, poly glycerol Sebacate or mixture there of The film gives superior support to the aberrant area of the viscous organ due to its effective adhering property. The polymer and knitted mesh material selection also depend on the material sensitivity towards the intimal layer of implant location and for that the guinea pig maximization test (GPMT) is a preferred method for the detection of skin sensitizers. It

belongs to the class of adjuvant-tests, where the substance will be applied in Freund Complete Adjuvant (FCA or CFA). The maximization test is based on the possible induction of an immune response of the skin during an induction period (at least 1 week). This pre-treatment of the subject will eventually result in a hypersensitive reaction during a further exposure, the so-called challenging phase. Skin sensitizers are substances that elicit an allergic response, such as allergic contact dermatitis, following contact with the skin. This study examined the effects of skin sensitisation on guinea pigs, including clinical signs of toxicity and mortality/morbidity, skin scorching observations, and the change in body weight. Four extract groups were used during the study. The degradation of polymer observed over a period of time for the clean transparency of the mesh. The study of degradation of polymer observed at temperature of 37 ± 2 ºC and 70 ± 2 ºC. Degradation has a significant impact on the stability and durability of polymer materials, which can have significant implications for product safety and dependability. The degradation mainly results in the formation of lower molecular mass products.

MATERIAL AND METHODS

The mesh prosthesis includes mesh layer and film layer. Polymeric solution is poured inside the glass substrate in order to commence the solvent casting method. The substrate is kept undistributed over a horizontal even surface for 0.5-04 hours at predefined temperature of 20-30 ºC. The film layer formed during the aforementioned step is subjected to adhesion and compression. The adhesive agent may be any medical grade adhesive including without limitation, loctite 4014 or dymax 213 – CTH or any polymer solution which helps to connect two different polymer layer without any structural deformation. The viscosity of solution may range from 0.1-1.5 dl/dg. The examples of polymer include without limitation, poly-L-lactide-co-caprolactone, poly caprolactone, poly-dl-lactic acid, poly glycerolse bacate or mixture thereof. The adhesive may be applied using various methods including, spray coating, dip coating, manually and evenly spreading the solution over mesh. The time of drying and compression of the mesh layer with the film mesh layer may range from 1-24 hours. The secondary annealing is carried out at a temperature ranging from 60-120 ºC, the time period ranges from 01-10 hour. Alcohol incubation may utilized any type of alcohol that is acceptable for medical use including without limitation, methanol, ethanol, propanol, iso-propyl alcohol and the likewise.

The mesh prosthesis is subjected to a process of formation of drainage holes. The drainage holes are formed on the bottom surface of the mesh layer of the mesh prosthesis. The time period for performing the process ranges from 1-24 hours. The predefined power of the machine may be in the range of 3-7 % and the predefined speed may be 17-23 %. The solution is kept at a temperature ranging from 50-150 ºC in a time period of 1 to 16 hour. Mesh prosthesis is first subjected to a radiation sterilization process, which may range from 5-30 kGy. The burst strength of mesh prosthetic may be measured using an instrument called Ubique Strength Tester. Figure 2 shows the transparency of the mesh and the hardness of the synthetic material used for the prosthesis. The hernia mesh was studied for *in vitro* degradation study for physiological and morphological studies. The study shows the degradation of the polymer film over the time which confirm visually during the each interval. Apart from this burst strength of the hernia mesh was play an important role after the implantation which need to track during the degradation study.

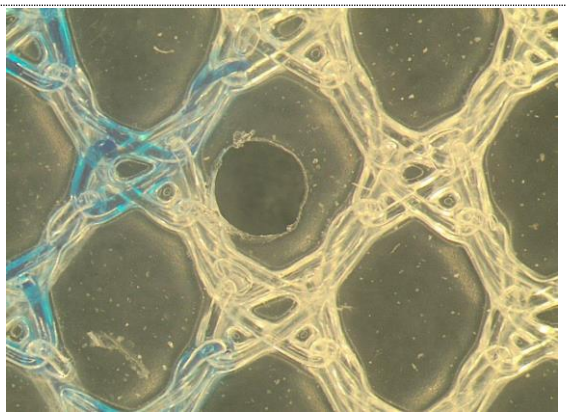

Fig.1 -Hernia Mesh with hole

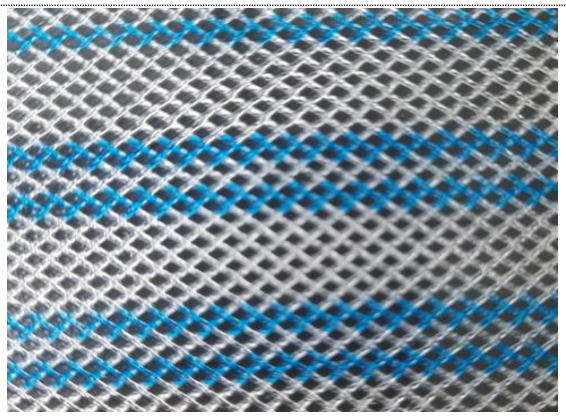

Fig.2 - Hernia Mesh Transparency

***In Vivo* study**

The skin sensitisation study of hernia mesh was conducted in guinea pig. The study of mesh comprised of four groups, G1, G2, G3 and G4 were designated as polar solvent control extract, polar test item extract, non-polar solvent control extract and non-polar test item extract, respectively. The group G1 and G3 consisted of 5 animals and the group G2 and G4 consisted of 10 animals. Polar and non-polar extract was prepared at extraction ratio of 6 cm^2/mL surface area/volume and incubated at 50 ± 2 ºC for 72 ± 2 hours. The study included an intradermal

injection on day 1, topical induction on day 8 and challenge on day 22. Fur from the designated sites for respective phases of the experiment was clipped closely using an electric hair clipper approximately 24 hours prior to initiation of the treatment

.

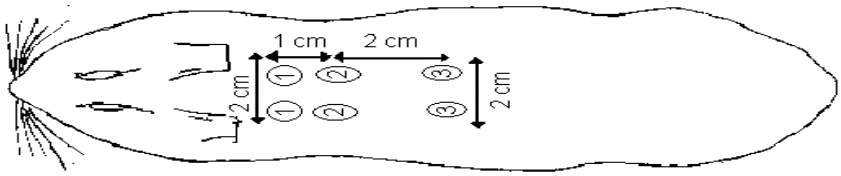

Figure 1: Site of intradermal injections in the Guinea pig for maximization test of Magnusson and Kligman

On day 1, the animals were injected at the shoulder region with 0.1 mL per injection of 3 pairs of intradermal injections. On day 7, intradermal induction sites of all the animals were treated (clipped area) with 0.5 mL of 10 % w/w Sodium Lauryl Sulphate in vaseline to produce local irritation. On day 8, the filter paper (2 cm x 4 cm) was saturated by soaking in polar solvent control, polar test item extract, non-polar solvent control and non-polar test item extract and applied topically to previously injected sites of G1, G2, G3 and G4 group animals, respectively. Similarly on day 22, the filter paper (2 cm x 4 cm) was saturated by soaking in the respective solvent controls and test item extracts and applied on to the respective groups over the pre-clipped area. The polar and non-polar solvent control and test item extracts were applied on the anterior and posterior part of right flank region for G1, G2, G3 and G4 groups, respectively. The test patch was held in its position for 24 ± 2 hours.

RESULT AND DISCUSSION

In Vitro Degradation Study

Polymer biodegradation is a process in which the polymer structure changes as a result of changes in polymer characteristics caused by the transformational activity of microbial enzymes, such as molecular weight decrease and changes in mechanical strength and surface qualities. The purpose of the mesh accelerated degradation study was to determine the mesh alien's burst strength and overall degradation time. Accelerated deterioration tests (ADT) are commonly used to evaluate the reliability of long-lasting items. Environmental stress promotes the depreciation of many items while also increasing the likelihood of catastrophic shocks. Polymer degradation is a change in a polymer's or a polymer-based product qualities, such as tensile strength, colour, form, and molecular weight, caused by one or more external elements, such as heat, light, chemicals, or any other applied force. The accelerated degradation study was performed at 70 ± 2 °C temperature. The real time degradation study was performed at 37 ± 2 °C temperature. The overall deterioration time is used to determine the mesh prosthesis' burst strength. Burst strength meaning here is the capacity of a material or object to maintain in continuity when subjected to pressure. Burst strength testing is useful because it allows producers to assess the package's strength and ensure that it is not destroyed during transit. The bursting strength value can be used to assess corrugated material quality. The chart 1 and 1.1 show the accelerated deterioration investigation, carried out at intervals of 0 to 12 days, with the peak burst strength measured between 11 and 12 kg/cm^2. The real-time deterioration investigation was carried out over a period of days, with the maximum burst strength range being 9-12 kg/cm^2. Another research of Accelerated Degradation was carried out at intervals of days ranging from 11 to 12 kg/cm^2.

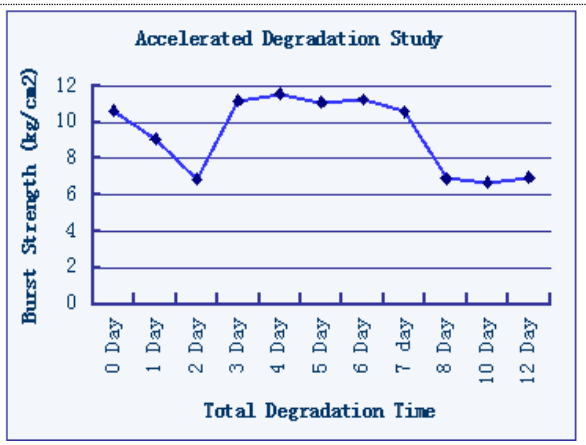

Chart 1. - Accelerated Degradation

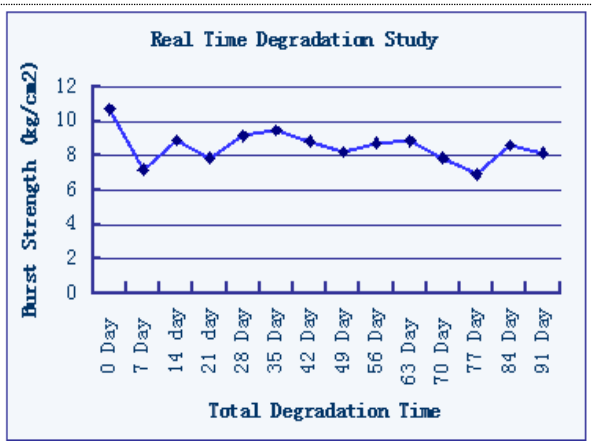

Chart 1. 1- Real Time Degradation

Toxicity and Mortality

All the animals were observed once daily for clinical signs of toxicity and twice daily for mortality. No clinical signs of toxicity and mortality were observed in any of the animals in all the groups.

***In Vivo* Skin Reaction Scoring Results**

I. Intradermal Induction (Day 1)

No treatment related skin reactions were observed at injection site 2 after intradermal injection at 24 ± 2 and 48 ± 2 hours observation in G1, G2, G3 and G4 group animals.

II. Topical Induction (Day 8)

No treatment related skin reactions were observed approximately at 1 hour and 24 hours after removal of the test patch in any of the animals of all the groups tested.

III. Challenge (Day 22)

No treatment related skin reactions were observed at (24 ± 2) and (48 ± 2) hours after removal of the test patch in any of the animals of all the groups tested. Evaluation of skin reaction was done by Draize (1959) method Refer table 1 for the skin scoring records.

Table 1. - Skin Scoring Records

Group, Sex Treatment	Animal No.	Site	Intradermal induction (Day 1)				Topical Induction (Day 8)	Challenges (Day 22)	
			24 ± 2 hr		48 ± 2 hr		1 & 24 hr	24 ± 2 hr	48 ± 2 hr
G1, Male & Polar Solvent contro	Gd 4171 to Gd 4175		Ery	Ede	Ery	Ede	Ery & Ede	RF Ant & Post	RF Ant & Post
		1	0	0	0	0	0	0	0
		2	0	0	0	0	0	0	0
		3	1	0	1	0	0	0	0
G2, Male & Polar Test Item Extr	Gd 4175 to Gd 4185	1	0	0	0	0	0	0	0
		2	0	0	0	0	0	0	0
		3	1	0	1	0	0	0	0
G3, Male & Non-Pol Solvent Control	Gd 4186 to Gd 4190	1	0	0	0	0	0	0	0
		2	0	0	0	0	0	0	0
		3	1	1	0	0	0	0	0
G4, Male & Non - Pc Test Item Extract	Gd 4191 to Gd 4200	1	0	0	0	0	0	0	0
		2	0	0	0	0	0	0	0
		3	1	1	0	1	0	0	0

Body Weight

The body weight of all animals observed on day 1 and 25. The chart no. 2 to 2.3 show the body weight of animals for all G1, G2, G3, and G4. There was no treatment related changes in body weight was observed. All animals showed normal physiological increase in body weights.

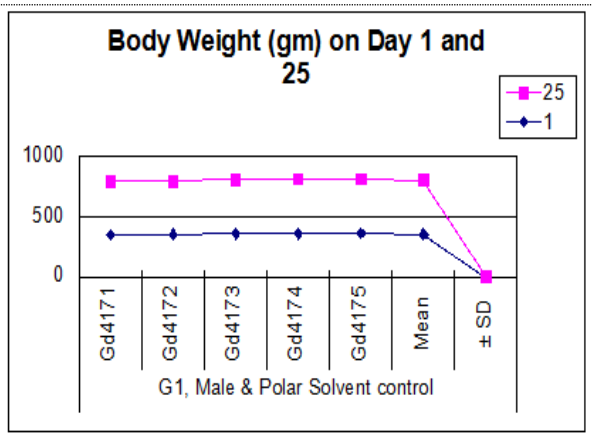

Chart 2.- Body weight of Group G1

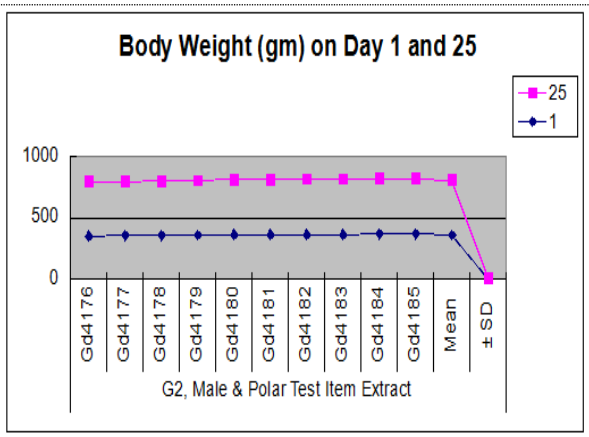

Chart 2.1. - Body weight of Group G2

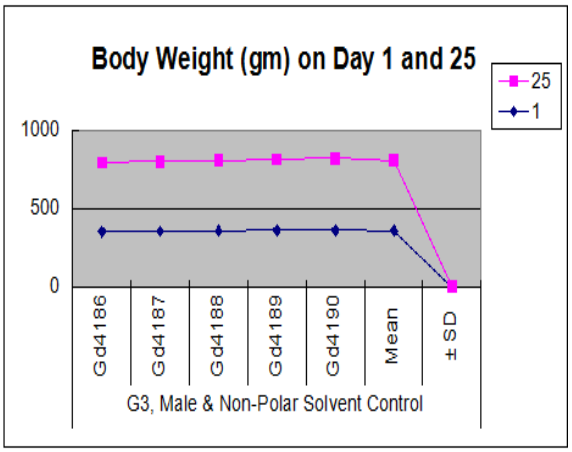

Chart 2.2. - Body weight of Group G3

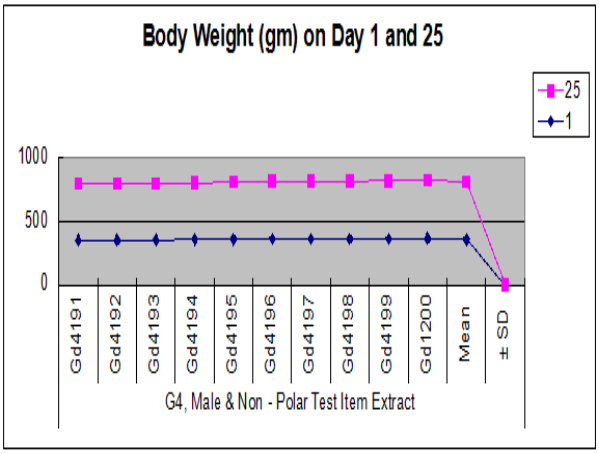

Chart 2.3. - Body weight of Group G4

CONCLUSION

Degradation strongly influences the stability and durability of polymer materials, which can have dramatic consequences in safety and reliability of products. The multicomponent mesh device was successfully obtained by coating a commercial hernia mesh with a nano structured membrane electro spun from a PCL-Gel blend. The polymer coated knitted mesh is used to repair hernias by providing a flexible scaffold. The positive morphological and physiological changes were observed. The polymer and knitted mesh material selection also depend on the material sensitivity towards the intimal layer of implant location and the guinea pig maximization test results. Additionally, no clinical signs of toxicity or mortality and body weight were observed in animals. Further this should be verified by implanting in animal model preferably swine or rabbit to confirm absorption, degradation, histopathological performance of the implant.

REFERENCES

I. Carmine W., Kim T., and Zhu D. Hernia Mesh and Hernia Repair : A Review. Engineered Regeneration. 2020 ; 1 : 19 - 33.

II. Luijendijik R. W., Wim C. J., Pettrousjka V. D. T., et al. A Comparison of Suture Repair with Mesh Repair for Incisional Hernia. The New England Journal of Medicine. 2000 ; 343 : 392 - 398.

III. Mudge M., and Hughes L. E. Incisional Hernia : A 10 year prospective study of incidence and attitudes. Br J Surg. 1985 ; 72 : 70 - 71.

IV. Helgstrand F., Rosenberg J., Kehlet H., Bisgaard T. Outcomes after emergency versus elective ventral Hernia Repair : A Prospective nationwide study. World J Surg. 2013 ; 37 (10) : 2273 - 2279. Doi : 10.1007/soo268-o13-2123-5.

V. Breuing K., Butler C. E., Ferzoco S., et al. Incisional ventral hernias : review of the literature and recommendations regarding the grading and technique of repair. Surgery. 2010 ; 148 (3) : 544 - 558. doi:10.1016/j.surg.2010.01.008.

VI. Montgomery A. The battle between biological and synthetic meshes in ventral hernia repair. Hernia. 2013 ; 17 (1) : 3 -11. doi:10.1007/s10029-013-1043-5.

VII. Martinez Serrano M. A., Pereira J. A., Sancho J., Argudo N., Lopez C. M., and Grande L. Specific improvement measure to reduce complications and mortality after urgent surgery in complicated abdominal wall hernia. Hernia. 2012 ; 16 (2) : 171 - 177. doi:10.1007/s10029-011-0875-0.

VIII. Derici H., Unalp H. R., Bozdag A. D., Nazli O., Tansug T., and Kamer E. Factor affecting morbidity and mortality in incarcerated abdominal wall hernias. Hernia. 2007 ; 11 (4) : 341 - 346.

IX. doi:10.1007/s10029-007-0226-3.

X. Landau O., and Kyzer S. Emergent laparoscopic repair of incarcerated incisional and ventral hernia. Surg Endosc Other Interv Tech. 2004 ;18(9) : 1374 - 1376.

XI. Shah R. H., Sharma A., Khullar R., Soni V., Baijal M., and Chowbey P. K. Laparoscopic repair of incarcerated ventral abdominal wall hernias. Hernia. 2018 ; 12 (5) : 457 - 463.

XII. Olmi S., Cesana G., Erba L., and Croce E. Emergency laparoscopic treatment of acute incarcerated incisional hernia. Hernia. 2009 ; 13 (6) : 605 - 608.

XIII. Yang GPC, Chan CTY, Lai ECH, Chan OCY, Tang CN and Li MKW. Laparoscopic verus open repair for strangulated groin hernias : 188 cases over 4 years. Asian J Endosc Surg. 2012 ; 5 (3) : 131 - 137.

XIV. Venara A., Hubner M., Le N. P., Hamel J. F., Hamy A., and Demartines N. Surgery for incarcerated hernia : Short term outcome with

or without mesh. Langenbeck's Arch Surg. 2014 ; 399 (5) : 571 - 577.

XV. Luijendijk R. W., Hop WCJ, Van den Tol MP, et al. A comparison of suture repair with mesh repair for incisional hernia. N Engl J Med. 2000 ; 343 (6) : 392 - 398.

XVI. Abdel Baki NA, Bessa S. S., Abdel R. AH. Comparison of prosthesis mesh repair and tissue repair in the emergency management of incarcerated para umbilical hernia : a prospective randomized study. Hernia. 2007 ; 11 (2) : 163 -167.

XVII. Bessa S., and Abdel R. A. Results of prosthetic mesh repair in the emergency management of the acutely incarcerated and/or strangulated ventral hernias : a seven year study. Hernia. 2013 ; 17 (1) : 59 - 65.

XVIII. Mandala V., Bilardo G., Darca F. et al. Some considerations on the use of heterologous prostheses in incisional hernias at risk of infection. Hernia. 2000 ; 4 : 268 - 271.

XIX. Kelly M. E., and Behrman S. W. The safety and efficacy of prosthetic hernia repair in clean contaminated and contaminated wounds. Am Surg. 2002 ; 68 (6) : 524 - 528.

XX. Carbonell A. M., Criss C. N., Cobb W.S., Novitsky Y. W. and Rosen M. J. Outcomes of synthetic mesh in contaminated ventral hernia repairs. J Am Coll Surg. 2013 ; 217 (6) : 991 - 998.

XXI. Andersen, K. E., Volund, A., and Frankild, S. The guinea pig maximization test—with a multiple dose design. Acta Derm. Venereol. 1995 ; 75 : 463– 469.

XXII. Basketter D. A., Dearman R. J., Hilton J., and Kimber I. Dinitro - halobenzenes : Evaluation of relative skin sensitisation potential using the local lymph node assay. Contact Derm. 1997b ; 36 : 97 - 100.

XXIII. Basketter D. A., Scholes E. W., Chamberlain M., and Barratt M. D. An alternative strategy to the use of guinea pigs for the identification of skin sensitisation hazard. Food Chem. Toxicol. 1995 ; 33 (12) : 1051 - 1056.

XXIV. Gerberick G. F., and Robison M. K. A skin sensitisation risk assessment approach for evaluation of new ingredients and products. Am. J. Contact. Derm. 2000 ; 11 : 65 -73.

XXV. Hofmann T., Diehl K. H., Leist K. H., and Weigand W. The feasibility of sensitisation studies using fewer test animals. Arch Toxicol. 1987 ; 60 (6) : 470 - 471.

XXVI. Kimber I., Basketter D. A. et al. Skin sensitisation testing in potency and risk assessment. Toxicol Science. 2001 ; 59 (2) : 198 - 208.

XXVII. Kimber, I. Skin sensitisation Testing in Potency and Risk Assessment. Toxicological Sciences. 2001 ; 59 (2) : 198–208. doi:10.1093/toxsci/59.2.198

XXVIII. Kligman A. M., and Basketter D. A. A critical commentary and updating of the guinea pig maximization test. Contact Dermatitis. 1995 ; 32 : 129 - 134.

XXIX. Momma J., Kitajima S., and Inoue T. The guinea pig skin sensitisation test revisited : An evaluation formula to predict possible sensitisation guinea pig skin sensitisation test and its use in a risk assessment process for human skin sensitisation. Toxicology. 1998 ; 61 : 91 - 107.

XXX. Robinson M. K., Gerberich G. F., Ryan C. A., McNamee P., White I. and Basketter D. A. The importance of exposure estimation in the assessment of skin sensitisation risk. Contact Derm. 2000 ; 42 : 251 - 259.

XXXI. Shaillaker R. O., Bell G. M., Hodgson J. T., and Padgham M. D. Guinea pig maximization test for skin sensitisation : the use of fewer test animals. Arch Toxicol. 1989 ; 63 (4) : 283 - 288.

XXXII. Steiling W., Basketter D., Berthold K., Butler M. et al. Skin sensitisation testing - new perspectives and recommendations. Food Chem Toxicol. 2001 ; 39 (4) : 293 - 301.

XXXIII. Th. Maurer; R. Hess. The maximization test for skin sensitisation potential—Updating the standard protocol and validation of a modified protocol. 1989 ; 27 (12) : 807–811.

XXXIV. Van der walle, Klecak H. B., Geleik H., and Bensink T. Sensitizing potential of 14 mono (meth) acrylates in the guinea pig. 1982 ; 8 : 223 - 235.

XXXV. Wahlberg J. E., and Boman A. Guinea Pig Maximization Test. Curr Probl Dermatol. 1985 ; 14 : 59 - 106.