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CNAS L2954

Final Report

Report Number: SDWH-M201904568-4 (E)

impression material

Oral mucosa Irritation Test

According to ISO 10993-10:2010
0.9% Sodium Chloride Extract

Sponsor: Zhengzhou Huaer Electro-Optics Technology Co., Ltd

Address: Floor 11, B of Building 18,the National University Science Park of Henan Province

Sanitation & Environment Technology Institute, Soochow University

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Content

Supplementary Explanation

(1) Please apply for rechecking within 15 days of receiving the report if there are any objections.

(2) Any erasure or without special inspection and testing seal renders the report null and void.

(3) The report is only valid when signed by the persons who edited, checked and approved it.

(4) The results relate only to the articles tested.

(5) The report shall not be reproduced except in full without the written approval of the institute.

Quality Assurance Statement

The Quality Assurance Unit inspected/audited this study in compliance with the following GLP regulations:
Good Laboratory Practice (GLP) Regulation 21 CFR Part 58, U.S. Food and Drug Administration (FDA). The laboratory is exempt from the following provisions: 21 CFR Part 58.105 Test and Control Article Characterization, and Part 58.113 Mixtures of Articles with Carriers.

The Quality Assurance Unit conducted inspections on the following dates. The findings were reported to the Study Director and to the Testing Facility Management. The final report was reviewed by the Quality Assurance Unit. The final report accurately describes the test methods in accordance with standard operating procedures, and the results are consistent with raw data of non-clinical studies conducted according to the study protocol.

Inspections	Date of Inspection	Date Reported to Study Director	Date Reported to Testing Facility Management.
Study Protocol	2019-11-13	2019-11-13	2020-01-13
Study Procedure	2019-11-19	2019-11-19	2020-01-13
Raw Data	2020-01-13	2020-01-13	2020-01-13
Final Report	2020-01-13	2020-01-13	2020-01-13

Quality Assurance Unit: Zhang Tao, Quality Assurance

2020-01-13 Date

GLP Compliance Statement

This study was fully in accordance with the technical requirements of the study protocol.

This study was conducted in compliance with Good Laboratory Practice (GLP) Regulation 21 CFR Part 58, U.S. Food and Drug Administration (FDA).

The laboratory is exempt from the following provisions: 21 CFR Part 58.105 Test and Control Article Characterization, and Part 58.113 Mixtures of Articles with Carriers.

Verification Dates

Test Article Receipt	2019-10-25
Protocol Effective Date	2019-11-13
Technical Initiation Date	2019-11-13
Technical Completion Date	2020-01-02
Final Report Completion Date	2020-01-13

Edited by: _____ 2020-01-13
Date

Reviewed by: _____ 2020-01-13
Study Director Date

Approved by: _____ 2020-01-13
Authorized Signatory Date

Sanitation & Environment Technology Institute, Soochow University

Summary

1 Test Article

Test Article Name	impression material
Manufacturer	Zhengzhou Huaer Electro-Optics Technology Co., Ltd
Address	Floor 11, B of Building 18,the National University Science Park of Henan Province
Model	Not supplied by sponsor (N/S)
Lot/Batch	N/S

2 Main Reference

ISO 10993-10:2010 Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization

3 Test Method

Irritation to oral mucosa of test article was evaluated using oral mucosa irritation test in the hamster in accordance with ISO 10993-10:2010 Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization.
Study protocol number: SDWH-PROTOCOL-GLP-M201904568-4.

4 Conclusion

Under the conditions of this study, the result showed that the irritations of the oral mucosa in the test group did not exceed those in the control group. And the irritation index for the test article on the hamster oral mucosa was 0.1. No significant evidence of causing oral mucosa irritation in the hamster was found.

Test Report

1 Purpose

The test was designed to evaluate the potential of a test article to cause oral mucosa irritation. This study was to determine the potential oral mucosa irritation after the leaching liquor of the test article contacted the hamster oral mucosa.

2 Reference

ISO 10993-10:2010 Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization
ISO 10993-12:2012 Biological evaluation of medical devices — Part 12: Sample preparation and reference materials
ISO 10993-2:2006 Biological evaluation of medical devices — Part 2: Animal welfare requirements

3 Compliance

Good Laboratory Practice Regulations, 21 CFR, Part 58.
ISO/IEC 17025:2005 General requirements for the competence of testing and calibration laboratories (CNAS—CL01 Accreditation criteria for the competence of testing and calibration laboratories) China National Accreditation Service for Conformity Assessment LABORATORY ACCREDITATION CERTIFICATE Registration No. CNAS L2954.
RB/T 214—2017 Competence assessment for inspection body and laboratory mandatory approval—General requirements for inspection body and laboratory Certification and Accreditation Administration of the People's Republic of China INSPECTION BODY AND LABORATORY MANDATORY APPROVAL Certificate No. CMA 180015144061.

4 Identification of Test and Control Articles

4.1 Test Article

Test Article Name	impression material
Manufacturer	Zhengzhou Huaer Electro-Optics Technology Co., Ltd
Address	Floor 11, B of Building 18,the National University Science Park of Henan Province
Test Article Initial State	Sterilized, UV sterilization
CAS Code	N/S
Model	N/S
Size	N/S
Lot/Batch	N/S
Test Article Material	vinyl polysiloxane
Packaging Material	Food grace PP
Physical State	Solid
Color	blue,white
Density	1.6
Stability	24 h<0.3%.336 h<0.3%
Solubility	0
Storage Condition	Room Temperature
Intended Clinical Use	Used for all crown and bridge, edentulous, orthodontic and implant impression techniques.

The information about the test article was supplied by the sponsor wherever applicable.
The Sponsor is responsible for all test article characterization data as specified in the GLP regulations.

4.2 Control Article

4.2.1 Negative Control

Name: 0.9% Sodium Chloride Injection (SC)
Manufacturer: Guangxi Yuyuan Pharmaceutical Co., Ltd.
Size: 500 ml
Lot/ Batch#: H19082605
Physical State: Liquid
Color: Colorless
Storage Condition: Room Temperature

5 Equipment and Reagents

5.1 Equipment

Equipment Name	Equipment Number	Calibration Expire
Constant temperature vibrator	SDWH217	2020-05-04
Autoclave	SDWH2097	2020-04-16
Electronic Balance	SDWH2061	2020-06-19
Electronic scale	SDWH442	2020-05-04
Biological Microscope	SDWH561	2020-03-26

5.2 Reagents

Reagent Name	Manufacturer	LOT
10%Formaldehyde	Sinopharm Chemical Reagent Co., Ltd	20181204

6 Identification of Test System

Species: Hamsters
Number: 6
Sex: male
Weight: 102~126 g
Health status: Healthy, not previously used in other experimental procedures
Housing: Animals were housed in groups in cages identified by a card indicating the lab number, test code and first treatment date
Animal identification: Stain with picric acid
Cages: Plastic cage
Acclimation Period: 7 days under the same conditions as for the actual test

7 Animal Care and Maintenance

Animal source: Suzhou Experimental Animal Sci-Tech Co., Ltd. <Permit Code: SCXK (SU) 2015-0007>
Bedding: corncob, Suzhou Shuangshi Laboratory Animal Feed Science Co., Ltd.
Feed: guinea pig diet, Suzhou Experimental Animal Sci-Tech Co., Ltd.
Water: drinking water met the Standards for Drinking Water Quality GB 5749–2006
Animal room temperature: 18~26°C
Animal room relative humidity: 30%~70%
Lights: 12 h light/dark cycle, full-spectrum lighting

Personnel: associates involved were appropriately qualified and trained
Selection: only healthy, previously unused animals were selected
There were no known contaminants present in the feed, water, or bedding expected to interfere with the test data.

8 Justification of Test System and Route of Administration

The Hamsters were used in this study because they have historically been used in safety evaluation studies and the guidelines have no alternative (non-animal) method. The species and number of animals as well as the route of administration used, are recommended by standard guidelines.
The test article was exposed to the test system through a solvent compatible with the test system. This was the optimal route of administration available in this test system.

9 Experimental Design

9.1 Preparation of Extracts

9.1.1 Pretreatment

No pretreatment required.

9.1.2 Extraction

Under aseptic conditions, samples were taken according to the sampling method (Mix the two samples at the ratio of 1:1 by equal weight and extract together (see the image in Annex 3)), and extracted in closed inert containers according to the extraction ratio of 0.2 g : 1 mL (sample: extraction vehicle). The extraction vehicle was SC.

Test Period	Actual Sampling	Extract Procedure			Final Extract
		Extract Ratio	SC	Condition	
Test extract	2.0 g	0.2 g : 1 mL	10.0 mL	50°C, 72 h	Clear
Negative control	/	/	5.0 mL	50°C, 72 h	Clear

The state of the extract did not change after extraction. The extract was stored at 4°C, and tested within 24 h, without the process of adjusting its pH value, filtering, centrifuging, diluting, etc.The vehicle (without the test article) was similarly prepared to serve as the control.

9.2 Experimental Procedure

Everted the check pouches. Washed the pouches with 0.9% Sodium Chloride Injection, and examined for any abnormality.
Soaked a cotton-wool pellet in the test article extract and placed it in one pouch of each animal. No sample was placed in the other cheek pouch, which served as a control.
The duration of exposure was 5 min. Following the exposure, removed the cotton-wool pellet and washed the pouch with 0.9% Sodium Chloride Injection, taking care not to contaminate the other pouch. Repeated the above procedure every hour for 4 h.
Treated the control animals similarly, using the negative control article alone.
Described the appearance of the cheek pouches for each animal and graded the pouch surface reactions for erythema according to the system given in **Table 1** for each animal at each time interval.

Table 1 Grading System for oral Reactions

Reaction	Numerical Grading
Erythema and eschar formation	—
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2

Moderate erythema	3
Severe erythema (beet-redness) to eschar formation preventing grading of erythema	4

Other adverse changes of the tissues should be recorded and reported.

9.3 Observation of Animals

At 24±2 h after the final treatment, examine the cheek pouches macroscopically, and humanely sacrifice the hamsters and remove tissue samples from representative areas of the pouches. Place in 10%Formaldehyde prior to processing for histological examination.

9.4 Evaluation of Results

9.4.1 Macroscopic evaluation

Compare the test cheek pouch with the cheek pouch on the contralateral side, The grades (**Table 1**) for each observation are added and the sum is divided by the number of observations to determine the average grade per animal (see **Table 4**).

9.4.2 Histological evaluation

The irritant effects on oral tissue shall be evaluated microscopically by a pathologist. The pathologist may grade each tissue according to the system presented in **Table 2.**

Table 2 Grading System for Microscopic Examination for oral Reaction

Reaction	Numerical Grading	Reaction	Numerical Grading
1. Epithelium	—	**3. Vascular congestion**	—
Normal, intact	0	Absent	0
Cell degeneration or flatting	1	Minimal	1
Metaplasia	2	Mild	2
Focal erosion	3	Moderate	3
Generalized erosion	4	Marked, with disruption of vessels	4
2. Leucocyte infiltration (per high power field)	—	**4. Oedema**	—
Absent	0	Absent	0
Minimal (less than 25)	1	Minimal	1
Mild (26 to 50)	2	Mild	2
Moderate (51 to 100)	3	Moderate	3
Marked (greater than 100)	4	Marked	4

Table 3 Irritation Index

Average Grade	Description of Response
0	None
1-4	Minimal
5-8	Mild
9-11	Moderate
12-16	Severe

Other adverse changes of the tissues should be recorded and included in the assessment of the response.

Subtract the control group average from the test group average to obtain the Irritation Index (see **Appendix**), consider any negative score as zero.

10 Results

Individual results of the test appear in **Table 4** and **Appendix**.

11 Conclusion

Under the conditions of this study, the test article impression material extract showed no significant evidence of causing oral mucosa irritation in the Hamster.

12 Record Storage

All raw data pertaining to this study and a copy of the final report are to be retained in designated SDWH archive.

13 Confidentiality Agreement

Statements of confidentiality were as agreed upon prior to study initiation.

14 Deviation Statement

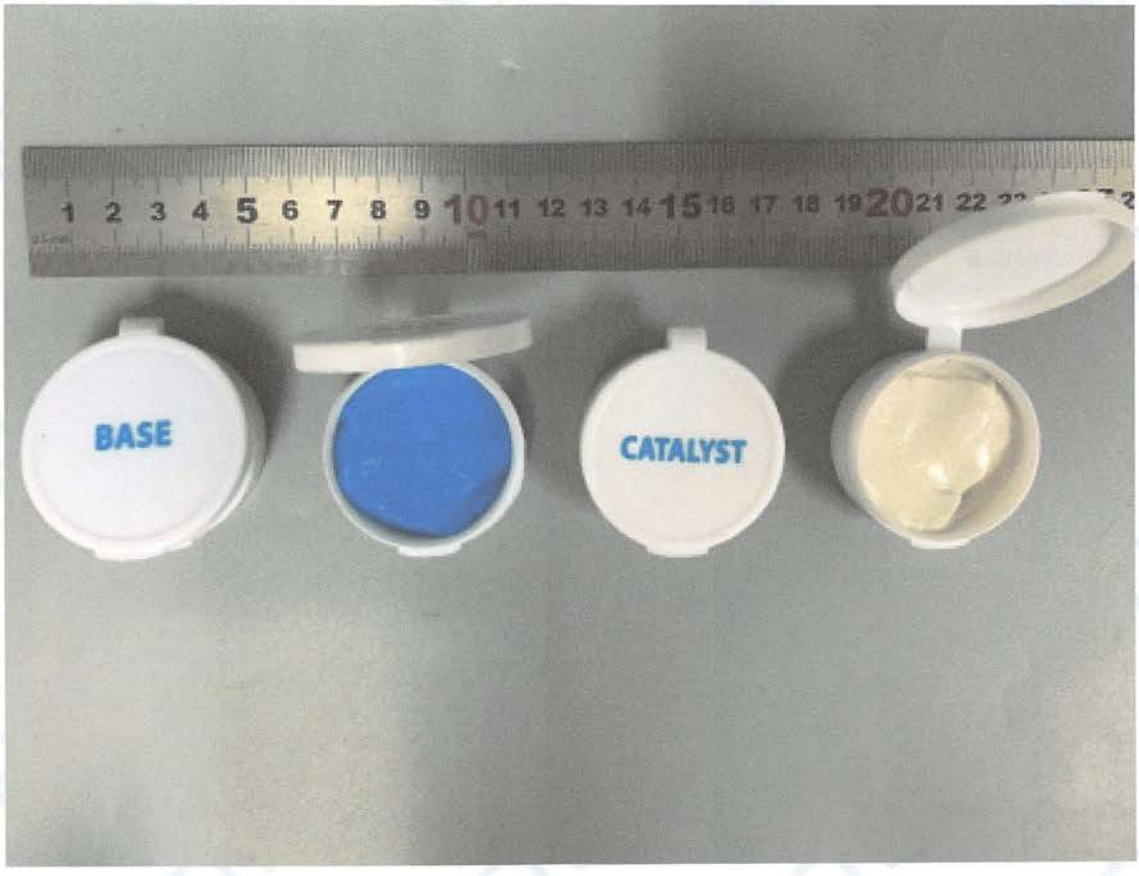
There were no deviations from the approved study protocol which were judged to have any impact on the validity of the data.

Annex 1 Test Data

Table 4 Macroscopic Evaluation

Group	Animal No.	Average Grading	
		Test	Blank
Test article group	1	0	0
	2	0	0
	3	0	0
Negative group	4	0	0
	5	0	0
	6	0	0

Annex 2 Photograph of Test Article



Annex 3 Information Provided by Sponsor

1 Production Process

Not supplied by sponsor.

2 Other Information

Not supplied by sponsor.

End of Report

Appendix
Histopathology Report of Oral Mucosa Irritation Test

Report Number: SDWH-M201904568-4(E)

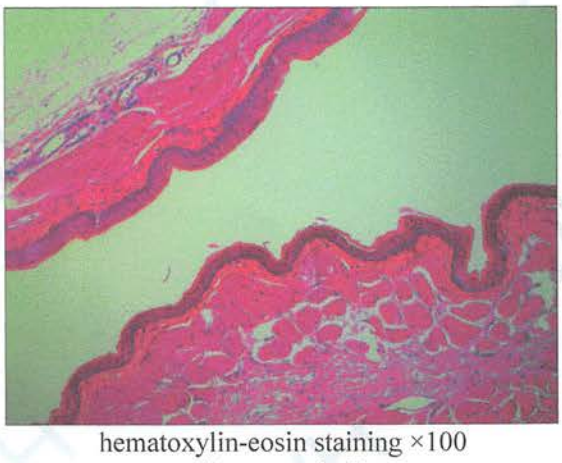
sample amount: 3 test samples and 3 test blank samples; 3 negative samples and 3 negative control blank samples.

Sample Preparation:

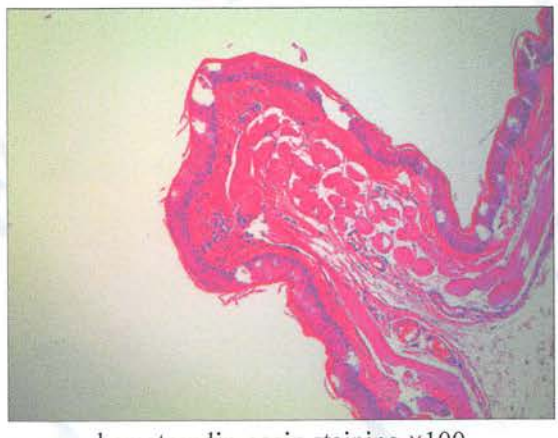
Tissue were preserved in 4% formaldehyde solution, after fixation, specimens were trimmed, embedded, sectioned and routine HE stained.

Histopathology Observation:

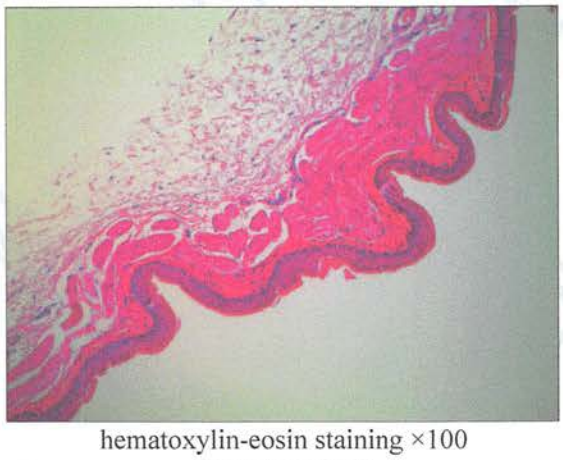
observed under microscope and tissue structure and histopathological change of test groups and control groups was compared their different.



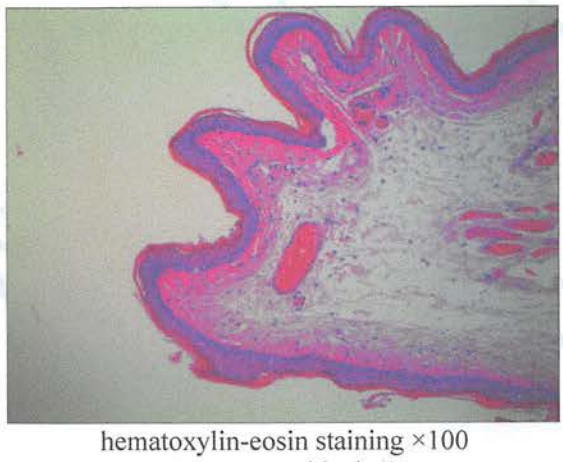
hematoxylin-eosin staining ×100
(Test sample 1)



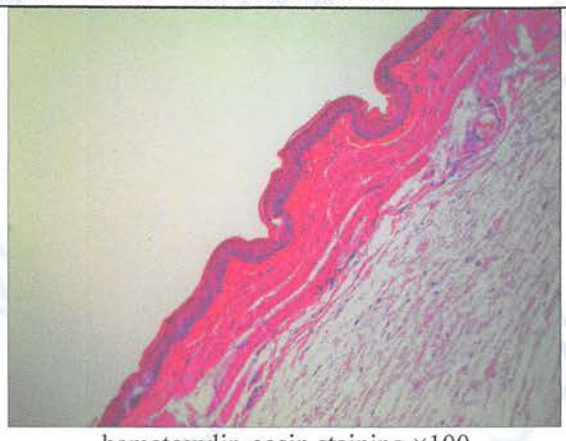
hematoxylin-eosin staining ×100
(Test sample 2)



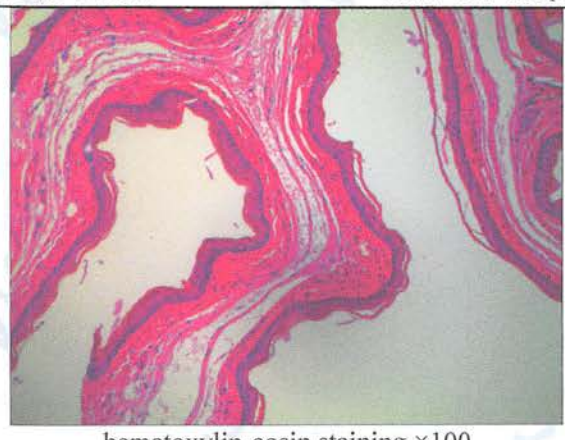
hematoxylin-eosin staining ×100
(Test sample 3)



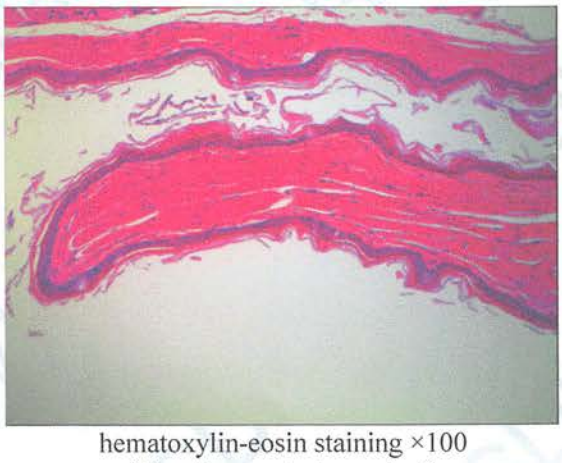
hematoxylin-eosin staining ×100
(Test group-blank 1)



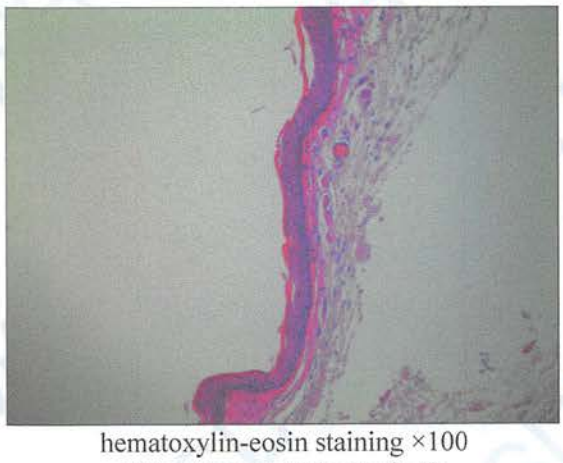
hematoxylin-eosin staining ×100
(Test group-blank 2)



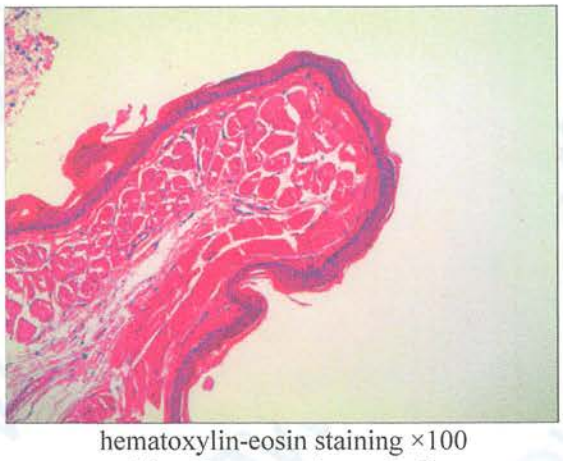
hematoxylin-eosin staining ×100
(Test group-blank 3)



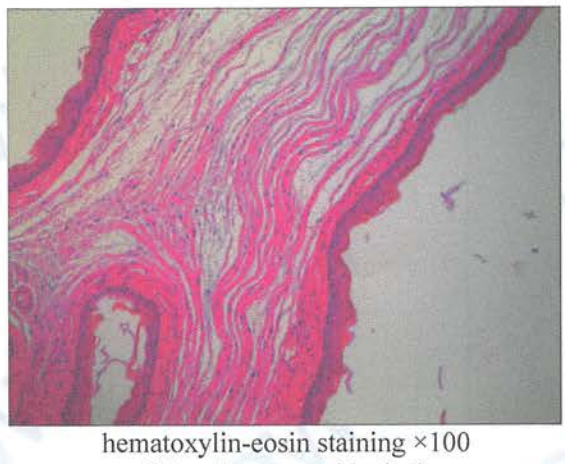
hematoxylin-eosin staining ×100
(Negative control sample 4)



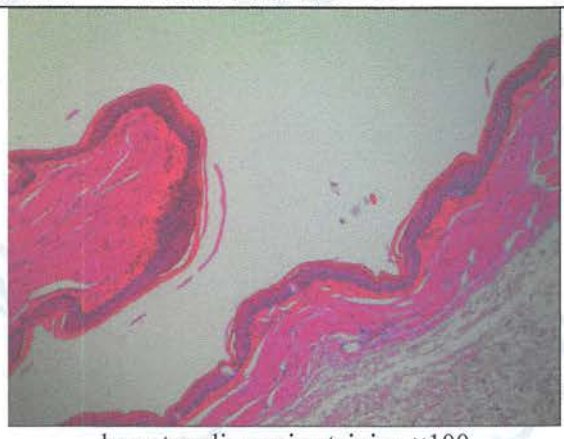
hematoxylin-eosin staining ×100
(Negative control sample 5)



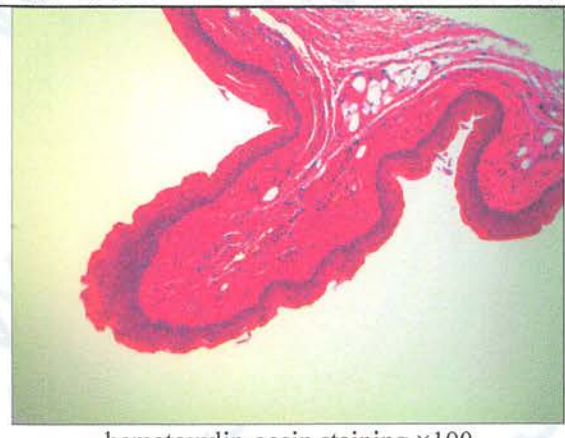
hematoxylin-eosin staining ×100
(Negative control sample 6)



hematoxylin-eosin staining ×100
(Negative group-blank 4)



hematoxylin-eosin staining ×100
(Negative group-blank 5)



hematoxylin-eosin staining ×100
(Negative group-blank 6)

Score for test group

No.	Observation	describe	Score
Test sample 1	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Minimal	1
	3. Vascular congestion	Minimal	1
	4. Oedema	Minimal	1
Test group/ Blank 1	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Minimal	1
	3. Vascular congestion	Minimal	1
	4. Oedema	Minimal	1
Test sample 2	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Minimal	1
	3. Vascular congestion	Minimal	1
	4. Oedema	Absent	0
Test group/ Blank 2	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Absent	0
	3. Vascular congestion	Minimal	1
	4. Oedema	Minimal	1
Test sample 3	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Minimal	1
	3. Vascular congestion	Minimal	1
	4. Oedema	Minimal	1
Test group/ Blank 3	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Minimal	1
	3. Vascular congestion	Minimal	1
	4. Oedema	Absent	0

Score for negative control group

No.	Observation	describe	Score
Negative sample 4	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Absent	0
	3. Vascular congestion	Minimal	1
	4. Oedema	Absent	0
Negative group/ blank 4	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Minimal	1
	3. Vascular congestion	Minimal	1
	4. Oedema	Absent	0
Negative sample 5	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Minimal	1
	3. Vascular congestion	Minimal	1
	4. Oedema	Absent	0
Negative group/ blank 5	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Absent	0
	3. Vascular congestion	Minimal	1
	4. Oedema	Absent	0
Negative sample 6	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Minimal	1
	3. Vascular congestion	Minimal	1
	4. Oedema	Minimal	1
Negative group/ blank 6	1. Epithelium	Normal, intact	0
	2. Leucocyte infiltration (per high power field)	Minimal	1
	3. Vascular congestion	Minimal	1
	4. Oedema	Absent	0

Histological Evaluation

—	Animal No.	Score		Average Grade
		Test	Blank	
Test group	1	3	3	0.4
	2	2	2	
	3	3	2	
Negative control group	4	1	2	0.3
	5	2	1	
	6	3	2	
Irritation Index				0.1

Irritation Index: Test article group - Negative control group = 0.1

Microscopically describe of organization:

1. The oral mucosal structure of test group and control group，stratified squamous epithelium and lamina propria，in normal condition. In stratified squamous epithelium，each layer of cells is normal and intact，can not see leucocyte infiltration、vascular congestion and oedema.
2. The lamina propria of test group and control group is normal and intact, leucocyte infiltration、vascular congestion and oedema can be seen in some groups.
3. In lamina propria of test group and control group, the Small blood vessel wall without edema, part of the tube concretions within a few red blood cells, Surrounding partial vessels can see the leucocyte infiltration.
4. The salivary glands can been seen in lamina propria of test group and control group, the structure of salivary glands is normal and intact，no enlargement of acinus, around acinus can not see leucocyte infiltration and oedema.
5. The skeletal muscle fiber under oral mucosa of test group and control group can not see the deformation、leucocyte infiltration and oedema.

Histopathologic diagnosis:

Non-irritant of oral mucosa

Slice reader: Weng Sohy

Professor of pathology

Date: 2020-01-13