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Skin Damage Due to Acrylic or Epoxy Adhesives

What causes rashes and itching?
How can they be prevented?

Introduction

A wide variety of adhesives are on sale today. These are presumed to be safe if they are used in accordance with the instructions that are described with the products.

However, since most of the constituents of adhesives are chemicals, they may have adverse effects on the human body when they are used inappropriately, and in some cases, even when the instructions for handling are followed properly.

Therefore, this issue will summarize the causes and provisions for the dermatitis caused by acrylic and epoxy adhesives that are commonly used in the industries, and that especially have many cases.

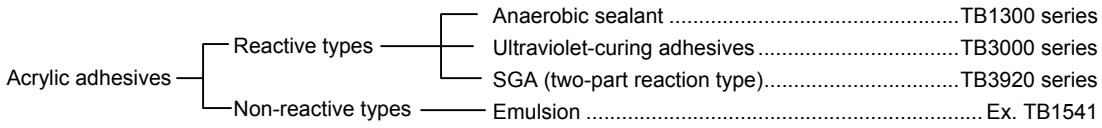
We hope this issue will provide you with some insights on the safe handling of adhesives.

Contents

1. Adhesive composition and skin damage

1-1. Acrylic adhesives

Acrylic adhesives can be largely divided into the following types.



Among these, ones that cause skin damage are mostly reactive types. Their major constituents are reactive (metha) acrylic monomers and oligomers, and they contain polymerization initiators and additives.

Some reactive monomers and oligomers are known to affect strongly skin and/or mucous membrane. Since contacting with that of high concentration for a short time, or that of low concentrations for a long time may result dermatitis, they often become problems in working places.

<Symptoms>

Generally, the type of skin damage referred to as a rash is mainly caused by chemical stimulation from direct contact with adhesives (primary skin irritation) and by the skin sensitization effect of the adhesive (allergic reactions; see Chapter 2). Symptoms vary depending on factors such as the individual's physiological constitution, properties of the chemical, and duration of exposure. In mild cases, symptoms consist of erythema (patches of skin reddening), papulation (bumps), tumefaction (red swelling), and itching. In severe cases, symptoms develop into edema (blisters) and lesions (sores) on the skin surface. In many cases, severe itchiness accompanies the symptoms, and scratching often worsens the condition.

Furthermore, a person who has previously acquired contact allergies to an adhesive tends to be extremely sensitive, and dermatitis may spread to areas that have not come into direct contact. This condition is known as systemic contact dermatitis. The sensitized skin may even react to minute amounts of resin or hardened resin that would otherwise be harmless under normal circumstances, and symptoms often persist.

<Dermatitic properties>

In terms of potential for skin irritation, chemicals with lower molecular weights tend to show greater skin penetrability in the case of direct skin contact, and thus have greater effects on the skin.

In the case of acrylic adhesives, the major agents of dermatitis are acrylic monomers with low molecular weights; these monomers are reactive dilutants added to improve workability. The above rule applies to acrylic monomers as well; those with lower molecular weights and with polarity tend to present greater potential for skin irritation.

In contrast, acryl polymers and emulsions (polymerized monomers lacking reactive groups) and acryl oligomers (which feature a reactive group but have high molecular weights) have low potential for skin irritation.

Table 1: Molecular weight of monomers and primary irritation index (PII)

Name of monomer	Molecular weight	PII
Tetrahydrofurfuryl acrylate	156	8.0
1,3-Butanediol diacrylate	198	8.0
Neopentyl glycol diacrylate	212	8.0
1,6-Hexanediol diacrylate	226	5.5
Trimethylolpropane triacrylate	296	4.6
Nonylphenoxy ethyl acrylate	318	4.2
Bisphenol A dioxy diethylene glycol diacrylate	452	0.8
Bisphenol A diglycidyl ether diacrylate	482	0.8
Dipentaerythritol hexa-acrylate	578	0.8

See Chapter 2 for details on PII.

Furthermore, metha acrylate, which shares the same structure as acrylate, has a significantly lower potential for skin irritation, and is considered to be an extremely safe compound. This is why it is used in dental and pharmaceutical products.

Table 2: Comparison of PII between acrylates and metha-acrylates

Types of (metha-) acrylate / Alcohol residue	PII	
	Acrylates	Metha - acrylates
1,3- Butanediol	8.0	0
1,6-Hexanediol	5.5	0.5
Neopentyl glycol	8.0	0
Tetrahydrofurfuryl alcohol	8.0	1.3
Benzoyloxy ethyl alcohol	3.3	1.4
Nonylphenoxy ethyl alcohol	4.2	1.0
Diethylene glycol	8.0	0.5

Since skin damage caused by sensitization differs from primary skin irritation, it is difficult to predict the severity of the resulting dermatitis. Even monomers with low potential for skin irritation may cause skin damage. The result depends largely on physiological constitution; more specifically, on whether or not the individual displays a positive reaction to the causative agent (allergen).

It is not always easy to determine whether the dermatitis caused by the use of adhesives is the result of direct contact with chemicals or an allergic response due to sensitization. Some individuals may even discover their sensitization to an adhesive for the first time only after handling it.

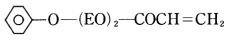
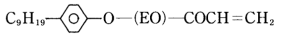
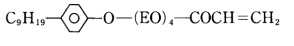
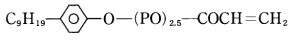
Thus, acrylic monomers and oligomers must be handled with care regardless of existing PII data.

<Improving the potential for skin irritation >

Currently, efforts are underway to develop acrylic adhesives with smaller PII values. These efforts are to:

1) select monomers with smaller PII values as constituents
2) substite metha-acrylates for acrylates as constituent monomers
3) use monomers with greater molecular weights, increased by the addition of 1-2 mols of ethylene oxide or propylene oxide.

Table 3: Improvement in PII by EO or PO modification

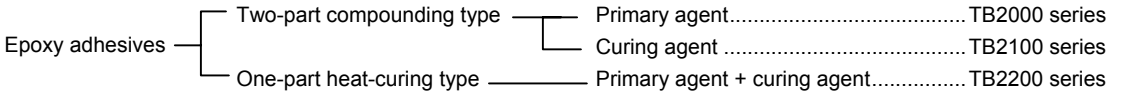
Molecular formula	P I I
	0.7
	2.0
	1.1
	0.6

However, a simple substitution of acrylate by metha-acrylate to reduce the PII value will result in an adhesive with entirely different properties, because the reactivity and polymer properties of metha-acrylates differ significantly from those of acrylates even though the two share a common structure. The same is true for modification by ethylene or propylene oxides.

Alteration of the monomer type in the formula needs complete re-investigation of the blend that will result in the required properties and standards of the finished product; this is a time and labor consuming process.

1-2. Epoxy adhesives

An epoxy adhesive is essentially a mixture of a primary agent and a curing agent.



(TB: Three Bond)

<Symptoms>

Symptoms are the same as for acrylic adhesives, such as erythema, tumefaction, and edema. As with acrylic adhesives, epoxy adhesives can also cause sensitization. Dermatitis resulting from an allergic response to acrylic adhesives is accompanied by intense itchiness.

<Dermatitic properties>

Both the primary agent and curing agent are potential skin damage.

Primary agent

The epoxy resin used in a primary agent usually consists of a low molecular weight epoxy compound that acts as a reactive dilutant. This compound is usually the cause of skin irritation and sensitization. As with the acrylic adhesives, compounds with lower molecular weights are believed to have higher potential for skin irritation.

Table 4: SPI of Epoxy monomer

Name of monomer	SPI classification
Phenylglycidyl ether	4
Butylglycidyl ether	4

See Chapter 2 for details on SPI.

Curing agent

Amines or organic acids are normally used as curing agents. Most are strongly active chemicals and have high potential for skin irritation.

- Amines: Primary and secondary amines have higher potential for skin irritation than tertiary amines, and fatty amines generally have higher potential for skin irritation than aromatic amines.

In contrast to liquid amines, which induce dermatitis even through short-term contact, solid polyamines and aromatic amines, which are polymers, cause similar degrees of skin damage only with more prolonged and serious exposure. Sensitization potentials differ largely among different amines, but polyamides are generally known to have lower potential for skin irritation.

Table 5: SPI values of amines

Types of amines	SPI classification
Diethylenetriamine	4.5
Triethylenetetramine	4.5
Diethylaminopropylamine	4.5
Xylylenediamine	4.5
m-Phenylenediamine	2
Polyethylene polyamine modification	
Ethylene oxide modification	2
Epoxy resin addition	-
Dicyandiamide	-

- Acid anhydrides: Many acid anhydrides also have high potential for skin irritation. Phthalic anhydride and maleic anhydride induce sensitization.

Table 6: SPI values of acid anhydrides

Types of acid anhydrides	SPI classifications
Dodecenylsuccinic anhydride	3
Tetrahydrophthalic anhydride	2
Hexahydrophthalic anhydride	2
Methyl endomethylene tetrahydrophthalic anhydride	2
Phthalic anhydride	-

As with acrylic resins, the sensitization-inducing properties of epoxy resins are problematic; appropriate care must be taken in their selection and handling, as stated previously.

Even individuals who do not take part in processes that involve direct contact with epoxy resins may become sensitized, simply by being in the same room as the resins.

A sensitized individual may become so allergic and may suffer skin inflammation through contact with minute amounts of unreacted epoxy resin that remain in the hardened resin.

2. Measuring the degree of skin damage

<Representation of the potential for skin irritation>

Indexes such as PII and SPI are commonly used to indicate the degree of skin damage caused by chemicals. These are used to assess primary skin irritation potential, and may be used as indicators for the degree of skin damage caused by direct contact with chemicals.

PII (Primary Irritation Index)

This index is widely used to represent the degree of skin damage caused by chemicals. PII is measured by the Draize method. The measured values are represented within a range of 0 to 8, with smaller scores indicating lower irritation potential.

However, large errors are observed in the PII values determined by the Draize method, and large deviations are seen, particularly in the scores for compounds with high potentials. Thus, the values should be only used broadly to identify the class of compound.

In Japan, compounds are normally categorized into three classes: PII values below 2 (low irritation potential), 2-5 (medium potential), and 6-8 (high potential).

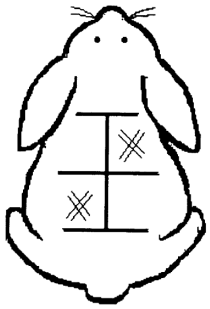
Table 7: PII evaluation table

PII	
I = 0	No irritation potential
0 < I ≤ 2	Slightly irritative
2 < I ≤ 5	Moderately irritative
5 < I ≤ 6	Moderately to severely irritative
I > 6	Severely irritative

Measurement of PII values (EPA Guidelines)

Fur is shaved off on the hip on the backside of six healthy white rabbits between 2.0-4.0 kg in body weight in order to make four 1 × 1 inch square areas on each rabbit. Two of the four area have intact skins and the remaining ones have abraded skins with small incisions made by surgical knife. Two patches, to which 0.5 ml of the sample has been applied, are then taped onto the opposite sides of the back. Observations are made after 24 and 72 hours to evaluate dermal reactions on a scale of 0 to 4 based on the evaluation criteria of conditions of erythema and edema formation. The mean score for all rabbits is calculated to obtain the PII value of the sample.

Conditions of sample application to rabbits and evaluation criteria



(1) Erythema and scab formation
- No erythema 0
- Slight erythema.....1
- Mild erythema 2
- Moderate erythema 3
- Severe erythema 4

(2) Edema formation
- No edema.....0
- Slight edema.....1
- Mild edema.....2
- Moderate edema 3
- Severe edema 4

Table 8: Examples of PII measurements and calculation method

Sex of rabbit	Erythema (E) and edema (O)	24 hours		72 hours		Mean
		Undamaged	Damaged	Undamaged	Damaged	
1 ♀	E	1	1	1	1	1.5
	O	1	1	0	0	
2 ♂	E	1	1	1	1	1.5
	O	1	1	0	0	
3 ♀	E	1	1	1	1	1.75
	O	1	1	1	0	
4 ♂	E	1	1	1	0	1
	O	1	0	0	0	
5 ♂	E	1	1	1	0	0.75
	O	0	0	0	0	
6 ♂	E	2	2	2	2	3.25
	O	2	1	1	1	

Given the above results, the PII values will be:
(1.5 + 1.5 + 1.75 + 1 + 0.75 + 3.25)/6 = 1.63.

* Another method for determining the PII value is seen in the Federal Register method, which uses an application area of 1.5 × 1.5 inches and exposure periods of 4, 24, and 48 hours.

SPI

This classification scheme was developed by the Epoxy Resin Formulators Division of The Society of The Plastics Industry in the U.S. to categorize the degree of skin damage caused by epoxy resin into six classes.

Table 9: SPI evaluation table

Classes	Irritation potential
Class 1	Virtually no irritability
Class 2	Weakly irritative
Class 3	Moderately irritative
Class 4	Strongly sensitizing
Class 5	Strongly irritative
Class 6	May be carcinogenic in animals

In contrast to the SPI, which is used solely to evaluate the effects of epoxy resins, the PII is applied to chemicals in general. However, there is no clear distinction as to which index is applicable for a given case; accordingly, numerous reports have evaluated the potential for skin irritation of epoxy resins using PII values.

Skin irritation potentials of commercial epoxy resins are normally represented by SPI values. Recently, however, the inappropriateness of evaluating both skin irritation and sensitization potentials using a single index has been pointed out; the use of SPI labeling tends to be declined.

<Skin sensitization potential>

Sensitization is the state in which a living body becomes highly responsive to exposure to certain chemical substances. In the case of handling adhesives, acrylic monomers and epoxy resins may enter the body through skin contact or vapor respiration and elicit allergic responses.

Once sensitized, an individual becomes highly responsive to even minute amounts of resin or vapor, and develops skin conditions such as rashes. Since this response is not the result of temporary skin irritation, the tendency to become sensitized does not coincide with the PII values, and thus, a different evaluation method is required. Prediction of sensitization potential is also rendered difficult by the fact that sensitization depends largely on the individual's physiological constitution.

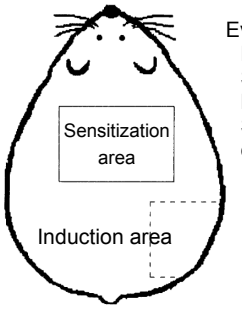
Sensitization testing

These tests check to determine whether the skin will become sensitized through repeated use of a chemical substance. The methods and the animals used for testing vary among different tests; below is an example of one such test.

Maximization test

In this method, two sensitization steps are taken. A guinea pig first receives a hypodermic injection of the sample and an application of a closed patch, and is then provided a recovery period before final exposure. This method has more effective detectability and reproducibility. It is also said easier to perform than other methods, since it requires shorter test periods.

Below is a summary of this method.



Evaluation:
No apparent abnormalities.....0
Slight or scattered erythema....1
Moderate erythema.....2
Severe erythema and edema.....3

An area of 4 × 6 cm is shaved above the shoulder blade of a healthy guinea pig weighing 300-500 g to prepare the sensitization area, and a hypodermic injection of 0.1 ml of the sample is administered. One week later, the area is shaved again and a sample, absorbed onto a piece of filter paper, is applied to the area as a closed patch for 48 hours using an impermeable bandage. An induction area is then prepared by shaving a 5 × 5-cm area on the abdominal region. Two weeks after the closed-patch application, a sample absorbed onto a piece of filter paper is applied to the induction area as a closed patch for 24 hours using an impermeable bandage.

The degree of skin damage should be judged based on erythema and edema formation at 24 and 48 hours after removal of the patch.

With this method, the technician should perform a comprehensive evaluation based on the ratio of the positively sensitized animals and the severity of the positive reaction.

Since the results of animal testing are not always applicable to humans, patch tests are sometimes performed on human subjects using methods similar to the maximization test.

However, in such cases, the dermal toxicity and irritation potential of the sample must be investigated prior to testing on human subjects, and the tests must be conducted with care under a doctor's supervision.

<Trends in toxicity testing>

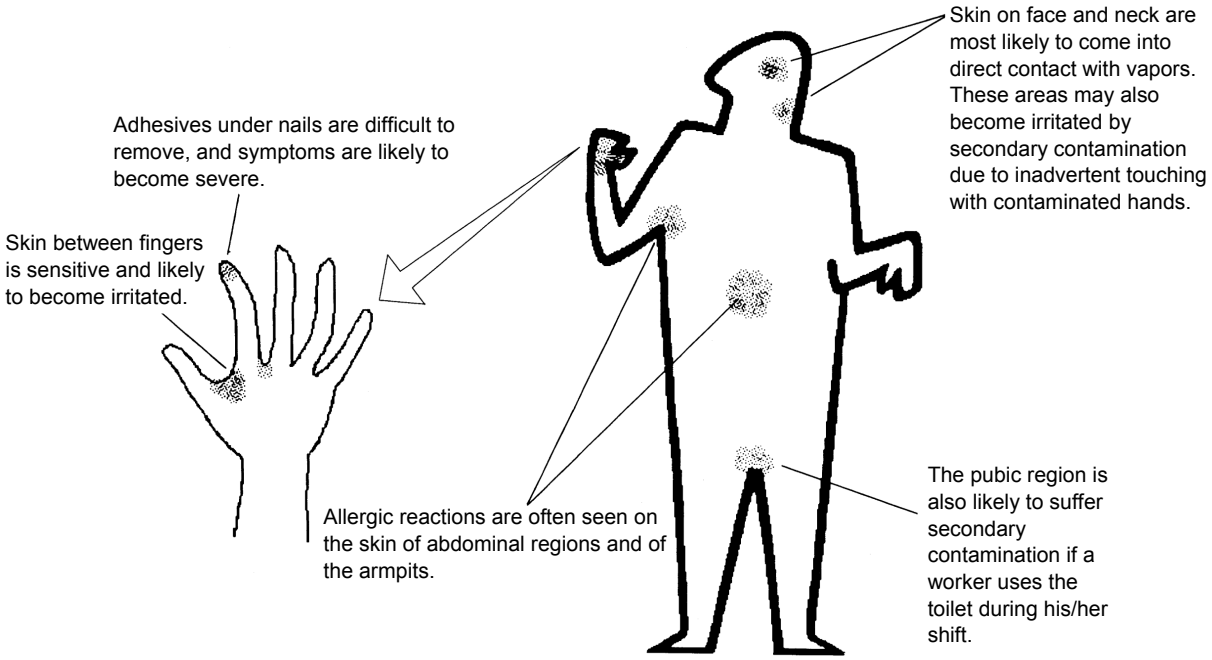
The methods described above all involve testing on laboratory animals. However, recent heightening in awareness of animal rights has led to strong opposition to such tests, and numerous studies are being conducted to develop ways to quantify the effect of chemicals on living bodies without using animals.

Systems to measure primary skin irritation and eye irritation using artificial proteins are available in the market, and their usage are progressively studied for the area of pharmaceutical, cosmetic, and industrial products.

3. Case studies of skin damage

Rashes have developed on skin although an automatic coating equipment was used.	Low molecular weight monomers and curing agents may adhere to the body as vapors. Install local exhaust systems to prevent the monomer vapor from spreading in the workplace.
Rashes have developed on skin after working near an irradiator for curing UV resin. Rashes have developed on skin after being at proximity of a dryer for curing epoxy resin.	The release of monomers is enhanced by the heat of reaction in resin curing and by the heat generated by irradiators or dryers. Keep in mind that vapors are released during the heating and curing processes. Position instruments and design exhaust systems to avoid exposure.
Body becomes itchy when wearing work suits. Rashes on skin worsen even when wearing protective gloves.	Monomers adhering to or absorbed by work suits may come into indirect contact with skin (secondary contamination). Protective gloves may actually induce skin rashes when worn on contaminated hands. In particular, tight-fitting gloves are more likely to cause sweating and opening of the pores, which causes skin to become more sensitive to monomers.
Severe skin rashes have developed even though the adhesive adhered to skin was thoroughly removed using a solvent.	Solvents accelerate the penetration of monomers into skin, resulting in acute skin inflammation, and should not be used to wash hands and skin.
In the past, rashes had developed from exposure to adhesives. Although adhesives are not handled in the present task, there is recurrent itchiness.	Allergic responses will recur in individuals who have developed sensitization to a chemical. When such recurrences are observed, remove the person from workspaces posing a risk of exposure to adhesives.

<Body parts susceptible to skin irritation>



4. Treatment and protection

<Treatment upon contact>

In the case of adherence to skin, wash adhesive off thoroughly with plenty of water and neutral soap. Do not use solvents to remove adhesive as this will accelerate penetration into skin and worsen skin damage. If symptoms such as itchiness persist even after 1-2 days, consult a medical specialist.

Dispose of clothing when it becomes severely contaminated. Ordinary work suits should be laundered by specialized laundry services and should not be washed at home.

<Protection>

Avoiding contact with adhesives is the best method for preventing skin irritation. Physical measures such as body protection and improved workspace design are thus required.

Protective gear

Protective gloves:

Select gloves made of impervious, solvent-resistant materials. Replace frequently.

Protective creams:

Creams are effective when used together with gloves. The protective cream may provide sufficient protection for extremely small amounts of exposure. However, even in such cases, hands should be washed immediately after completion of work.

Protective clothing:

Wear long-sleeved work suits. Use laboratory aprons and sleeves when necessary.

Workspace improvements

Ventilation:

To prevent contamination of air by monomer vapor, establish engineering measures such as sealing of instruments and installation of general and local exhaust systems to provide proper ventilation.

Cleaning:

The workspace should be well ventilated and kept clean. Surfaces and clothing that have come into contact with adhesives should be cleaned immediately. Adhesives may be wiped off using commonly available organic solvents and are especially soluble to ketones (acetone, methylethyl ketone, etc.).

Have a large supply of disposable gloves and cloths on hand, and replace them frequently.

Automation:

To reduce the chance of contact with adhesives, promote automation of facilities.

<Considerations for workers>

There is no reliable method of predicting whether an allergic reaction will be elicited in a worker. To limit the damage caused by a worker's exposure to monomers, the worker's allergy history should be given thorough consideration, and the worker should be swiftly transferred if develops any symptoms.

Workers should also be fully notified of the safety procedures, and education and training should be conducted regularly. Caution signs should be posted in appropriate areas of the workspace, and workers should be fully familiarized with the rules and regulations governing exposure prevention.

Concluding remarks

Above we have provided a summary of the general nature of skin damage caused by exposure to acrylic and epoxy adhesives, and discussed a number of preventative measures.

Currently, in the chemical industry, new products and new applications that are not restricted to adhesives are continually being developed and introduced into the workplace.

Given these circumstances, we believe it is our duty as an adhesives manufacturer to carry out constant studies on the hazardous properties of the relevant constituents and to notify our customers of exposure prevention measures in order to avoid the health problems of workers and environmental pollution. We also ask that our customers become fully knowledgeable as to the characteristics of these products before using them.

In recent years, there has been an explosion of information regarding the toxicity of chemical substances and related occupational health and safety issues. We hope that our efforts as adhesive manufacturers and the care taken by our customers to promote the proper handling of our products will enable widespread application of our superior adhesives while avoiding any associated health hazards.

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