REVIEW ARTICLE

Adverse Effects of Colophony

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Abstract: Regarding colophony, the use in industries, adverse effects, diagnosis, pathophysiology and control are reviewed. Colophony is an unhomogeneous mixture of resin acids as like abietic acid and neutral substances. Colophony is used everywhere, in industry, daily life and medical supplies. Soldering workers are exposed to the colophony fumes heated up to the temperature of soldering irons. The effects of exposure to colophony are classified into bronchial asthma and contact dermatitis. Colophony fumes cause bronchial asthma by its nonspecific irritation. Inhalation challenge test and repeated spirometry during working day may help the diagnosis of colophony induced asthma. Improvement of working environment for soldering and development of new flux instead of colophony will be necessary. A study on contact dermatitis revealed that colophony and its related compounds are one of major causes for contact dermatitis. Cases of dermatitis by depilatory agents used to remove hair from slaughtered swine, anti-slipping cream for ballet shoes or resin for cello strings have been reported. Patch test may contribute to the diagnosis of dermatitis caused by colophony.

Key words: Colophony, Bronchial asthma, Contact dermatitis, Soldering, Rosin

1. Chemical Characteristics of Colophony

Colophony, also known as rosin or pine resin, is a yellowish residue appearing after distillation of oleoresin obtained from plants belonging to Pinaceae (mainly Pinus genus). Generally used colophony involves gum rosin (obtained from scratching the bark of pine), wood rosin (obtained from stumps), and tall oil rosin (obtained from the black liquid generated during pulp paper processing as a byproduct)¹-². Colophony is an unhomogeneous mixture of approximately 90% resin acids and 10% neutral substances but its precise constituents are not known. The reason for this is that the constituents vary with species extracted, climate, extraction method and storing method²-³. The resin acids involve abietic acid, dehydroabietic acid, neoabietic acid, and isomers like dand iso-d-pimaric acid. The neutral substances primarily include stilbene compounds and other hydrocarbons³. The resin acids are monocarboxilic acids with alkylated hydrophenanthrene nucleus and can be classified into 2 types; the abietic acid type characterized by conjugated double bond and the pimaric acid type without conjugated double bond.

2. Use of Colophony

Colophony is used everywhere e.g. depilatory agents, shoes, medical adhesive tapes, resin for stringed instruments,
medicine for warts, soldering flux (paste), cutting oil, telefax papers, putty used in iron foundries, Duraphat (fluoridizing varnish), adhesives, paints, and glues.

Solder, which is widely used in the field of electronics, in particular, contains a small amount of colophony in the paste, resulting in the prevention of solder oxidation, better spreading and flux of solder. It is also known as a prominent flux by its physicochemical characteristics (non-erosive action, non-conductivity, and hydrophobicity). Furthermore, resin acids are hydrogenated or esterified in the presence of glycerol, pentaerythrol, ethylene glycol to form colophony compounds, which are widely used in industry.

Papers based on mechanical pulps that are considered to be environmentally friendly have a greater potential to elicit positive patch test reactions than papers made from other pulps.

3. Effects of Exposure

Since colophony is used in a variety of areas as mentioned previously, many clinical cases related to colophony have been reported. According to the reports, the symptoms caused by colophony use are classified into bronchial asthma and contact dermatitis.

1) Bronchial asthma

In electronic parts factories, soldering workers are exposed to the colophony fumes heated up to the temperature of soldering irons (350–400°C). It is already established that colophony is related to bronchial asthma with the disease rate of 4–20%.

Precise constituents of the fumes are not definite, but thought to consist of nonspecific irritants on respiratory organs like resin acids and their decomposed products, which are assumed to cause bronchial asthma.

Some reports described cases where soldering workers developed chronic coughs and respiratory difficulties which were suspected to reflect operation-induced allergic alveolitis based on results from chest X ray, pulmonary function tests and bronchoalveolar lavage.

It is known that some feather plucking workers also develop asthma. Test of hypersensitivity revealed that the patients are negative to feathers themselves but colophony used in the plucking process of feathers is responsible for that symptom. Furthermore an inhalation challenge test showed that workers in tire factories develop asthma by a mixed solution of tall oil and pine resin used as a glue.

In order to study these findings further, the relationship between an increase in bronchial responsiveness and delayed asthma during inhalation of toxic substances in work sites was examined by a histamine inhalation test performed on control groups and exposed groups. It was shown that responsiveness markedly increased 3 hr after the exposure, followed by development of delayed asthma. Thus it was shown that delayed asthma was induced by an increase in bronchial responsiveness, presumably an inflammatory mechanism.

2) Dermatitis

While contact dermatitis induced by colophony in soldering flux (paste) is widely known, dermatitis by colophony in various other fields have been reported. Cases of dermatitis by depilatory agents used to remove hair from slaughtered swine, anti-slipping cream for ballet shoes, or resin for cello strings have been reported. Similar cases have been reported for gardeners who replant pine saplings without wearing gloves, secretaries handling large amounts of telefax papers in office, workers using putty in iron foundries, an accordion repairman using wax in repairing and tuning accordions, or turners handling cutting oil. Most of these patients tend to have their dermatitis mitigated while they are away from their work and it recurs when they are back to their work.

Adhesive tapes are known to cause symptoms. Medical adhesive tapes applied to patients wounds or resin acid compounds in adhesive plasters cause symptoms in some people involving those who do not have skin problem histories.

Since allergic contact dermatitis due to anti-wart agents has been reported, it is expected to check whether a patient is allergic to colophony before using these agents. Furthermore stomatitis induced by Duraphat, an anti-decayed tooth agent, or a glue used to repair broken dentures has been reported.

Other reports described a case of allergic urticaria from colophony observed after using paste and implication of light hypersensitivity in colophony-induced dermatitis. A case of dermatitis on her forehead and round the mouth following treatment for acne with an Australian tea tree oil was reported.

4. Epidemiology of Colophony-Induced Health Disorders

A study on contact dermatitis revealed that colophony and its related compounds are one of major causes for contact dermatitis. Actually they were the 4th most frequent cause
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to make the patch test positive\textsuperscript{35}. It is assumed that explanation of allergy solely based on patient’s history is difficult since colophony is used everywhere.

A residents study performed to elucidate a cause for palm eczema revealed that an occupation-related antigen in female office workers was colophony. In a study on general residents in a city, the most frequent cause for eczema was a history of eczema in childhood followed by being female, occupational exposure, histories of asthma or pollinosis, and working for service industries, in this order\textsuperscript{36}.

A follow-up study on respiratory symptoms of retirees from electronic parts factories revealed that the ratio of retirees due to health problems was higher in soldering workers compared to that of storekeepers or office workers. And their work-related respiratory diseases accounted for major quitting reasons\textsuperscript{37}.

In order to check work-related respiratory diseases in workers in an electronic parts factory, inquiries and lung function test were performed, demonstrating that 22% of workers exposed to soldering fumes had respiratory difficulty or stridor\textsuperscript{38}. It is highly possible that these symptoms were caused by colophony fumes.

A paste inhalation challenge test and a follow-up study were performed in workers in another factory. It was shown that work-related asthma induced nonspecific bronchial hypersensitiveness to histamine inhalation and indirect exposure to paste during work delayed recovery from histamine reaction. Persisting symptoms probably stem from exposure to colophony or incomplete clearance of colophony from lungs\textsuperscript{39}.

A study on ratios of workers with work-related respiratory diseases in the process of manufacturing solder was performed. The workers were categorized into 3 groups based on concentrations of colophony in the respiratory zone. The ratio of work-related asthma was 21 and 4% for the high/medium and the low exposure group, respectively. In accord with intensity of exposure, mean values of forced expiratory volume in one second (FEV\textsubscript{1}) and FVC decreased and values of serum IgM concentration were in the following order; control workers<solder manufacturers<soldering workers. A previous study on soldering workers demonstrated that 1/3–1/2 workers had respiratory symptoms in accord with serum IgM levels. The research report suggested that the symptoms developed unless the level of resin acids in fume were within some limited values\textsuperscript{40}.

Medical examination by interview, clinical chemistry, pulmonary function, and olfactory test was performed on soldering workers and control workers. The degree of exposure was evaluated by both exposure concentration and time. It was found that colophony fume at concentrations above 0.1 mg/m\textsuperscript{3} was likely to evoke dried nose, respiratory difficulty, and bronchial asthma\textsuperscript{41}.

Common skin lesions were found in one third of opera-house artists and more than 50% had a history of intolerance to cosmetics. However, colophony gave positive patch test reactions in only 3 subjects among them\textsuperscript{42}.

5. Pathophysiology

The mechanism where mixtures of small molecule compounds like colophony induce bronchial asthma is still not clear. The study on work-related asthma is important in the treatment and prevention of the disease and the search for the disease model\textsuperscript{43}.

When colophony is heated it is decomposed into numerous small molecule substances (aldehydes and carboxylates). Thus in the past allergens of colophony were thought to be decomposed products of colophony. But at present major allergens are supposed to be resin acids based on a report demonstrating that work-related asthma is induced by resin acids in factories. In the report, a large amount of resin acids was detected in the air since colophony was heated at a low temperature of 140°C where decomposition proceeded slowly. In addition, degradation takes place which leads to the creation of different oxidation products possessing a more or less distinct sensitizing power\textsuperscript{44}.

While certain time lag exists between the first exposure to colophony and the development of symptoms, longer exposure period promotes the development. The results from an experiment showed that there was a weak correlation between colophony and results of histamine release test and atopic patients are more susceptible than non-atopic subjects. In addition, smokers have great probability to develop asthma presumably through nonspecific injury of the respiratory mucosa\textsuperscript{7, 45}. Furthermore abietic acid was found to injure epithelium of alveoli, trachea, and bronchi, promoting pulmonary disorder\textsuperscript{46}. Since subjects with highly exposed history or symptoms have higher serum values of IgM or IgE, it is possible to forecast development of respiratory symptoms in subjects with highly exposed history as well as high values of these serum parameters. It was reported that besides asthma an increase in serum IgM did not occur\textsuperscript{7}.

6. Diagnosis

Early diagnosis is possible when information concerning
mechanism for development of respiratory diseases or sites where contact with causing substances occurred.47>

1) Inhalation challenge test

In an inhalation challenge test performed on paste handling workers with respiratory symptoms in an electronic parts factory, many workers were found to be positive48~. Thus hypersensitivity caused by colophony fumes was demonstrated49~.

Another inhalation test was performed on 34 workers with work-related asthma and 17 with respiratory symptoms in another factory. All the positive responders after exposure to colophony within 15 min presented a marked decrease in FEV1. When the positive responders were exposed to Portuguese Y colophony and American WW colophony on the same condition, the response to the former was greater than that of the latter, demonstrating that methylation of the carboxyl group of colophony made responses smaller50~.

2) Spirometry

In a British electronic parts factory, inquiries and spirometry were performed on 104 soldering workers (93 females and 11 males). For a duration of 15 months, 68 workers used only solder containing paste and 36 widely used paste and non-colophony water soluble substances. As a result, approximately half of the subjects developed irritant symptoms in eyes, throat, pharynx, and nose, provoking respiratory symptoms such as cough, sputum, and stridor more frequently than general subjects. Spirometry was performed on Monday morning prior to work when pulmonary function did not drop. It was reported that slight decreases in FEV1 and vital capacity (VC) were observed after work and the decreases did not correlate with the amounts of solder used in the work51>

Furthermore, peak expiratory flow (PEF) recording was performed on 22 workers with colophony-related asthma in an electric factory at 1–2 hr intervals during both working hours and non-working hours, showing the seasonal change in 4 subjects who underwent the study approximately a year. PEF values in winter were obviously lower than those in summer. There was also a difference between PEF values in working hours and those in non-working hours; the amplitude of PEF values increased during working hours and the acrophase became faster. Thus the effect in the pulmonary function caused by the exposure to colophony was demonstrated52.

In another study, 29 subjects with respiratory symptoms related to colophony exposure underwent PEF measurements from rising to bedtime at a 1 hr interval. The results were then analyzed with regard to the occupational history and the inhalation challenge test, revealing physiological pattern of asthma attacks from daily mean, maximal and minimum PEF values. Continuous working increased asthmatic attacks, and 1–3 days were required for recovery. The results from the PEF recording correlated well with those from the inhalation challenge test demonstrating that it is an appropriate method to diagnose moderate asthma. The records of PEF are used to screen subjects who have symptoms not related to work53~.

3) Patch test

It was reported that compared to the usual 20% colophony patch test, the patch test containing neutral colophony screened out more positive subjects with a ratio approximately more than 40%54, 55).

A case was reported in which a subject was negative to abietic acid but positive to abietic alcohol, abitol hydride or Foral 85 (a glycerol ester of abietic acid hydride)56~. Thus the negative response to the patch test does not necessary deny the possibility of occupational allergy. The reason for this is that patches sometimes contain small amount of active ingredients since rosin commonly used in patches is 20% gum rosin in Vaseline and rosin is produced in different sites. A report suggested that active ingredients in patches are too low to obtain positive responses56>. Therefore the test should be performed with compounds which are practically used.

The sensitizing capacity of 7 commercial modified-colophony products of different origins were studied experimentally in guinea pigs and all products showed a weak sensitizing power, but a moderate to strong irritant effect57~.

7. Clinical Course

Symptoms of workers subside after work, but usually followed by incomplete recovery to the normal level. Thus many people try to find jobs without exposure to colophony. A study reported that there is a better chance to return to the normal health state after quitting job than working at the same work site7~. In the cases where symptoms continue after quitting job, it is likely that subjects are exposed to colophony in their surroundings. Indeed, colophony is contained in various goods for daily use. Colophony has been detected in the air around pine trees. Asthmatic attacks, therefore, may occur in subjects with symptoms just after
walking through pine trees or bringing Christmas trees in. There are many serious asthmatic attacks which threaten patient’s lives. Exercise is critical to induce attacks in some cases. For some patients, light exercise such as shopping precipitates attacks, resulting in need for someone to help shopping.

8. Control

While bronchial asthma has immunological characteristics, immunological sensitization has not been proven by skin test or in vitro experiments. However, chemical survey on allergens like colophony has been useful in the prevention and the control of the drug-allergy.

Moreover, in order to estimate exposure concentration of colophony accurately, a new method to measure colophony fumes is required. In a method currently recommended, contents of aldehydes (decomposed products by heat) in fumes are measured. There is a report indicating that a correct measurement of colophony is performed by resin acids which are produced from condensation reaction of unsaturated double bonds.

Critical values of decomposed products of colophony are determined by MBTH (Methyl 1-2-benzthiazon-hydrochloride) method, indicated as total fatty aldehydes, and are calculated as formaldehyde.

On the basis of the sensitizing effects of colophony, ACGIH recommended to reduce exposure to as low as possible.

It is also important to control and reduce exposure to lead as well as colophony contained in solder and toluene diisocyanate (TDI) produced from polyurethane enamel, a covering material, in soldering work.

In order to detect workers under the influence of colophony, medical examination before and during working should be performed with a focus on allergic history, family history and smoking history. Inquiries also should be done on when, where or in which situation symptoms occur. These information must be utilized for the control of working environment. For that purpose, improvement of environment in working sites for soldering and development of new flux (those causing less symptoms) instead of colophony will be necessary. Actually, cutting oil prepared from vegetable oil is now in the process of development. In addition, allergenicity of rosin was considerably reduced by hydrogenation or esterification with glycerol.

References

17) Aberer W (1987) Allergy to colophony acquired...
backstage. Contact Dermatitis 16, 34–6.


23) Fregert S (1979) Colophony in cutting oil and in soap water used as cutting fluid. Contact Dermatitis 5, 52.


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51.
60) ACGIH (1995) 1995–1996 Threshold Limit Values (TLVs) for chemical substances and physical agents and Biological Exposure Indices (BEIs).