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## Demographic and clinical profile of occupational cases of sensitization to methylisothiazolinone and Kathon CG: a cross-sectional study

*Perfil demográfico e clínico de casos ocupacionais de sensibilização a metilisotiazolinona e Kathon CG: estudo seccional*

### Abstract

**Introduction:** methylisothiazolinone alone or associated with methylchloroisothiazolinone (Kathon CG) is a preservative related to occupational allergic contact dermatitis. **Objectives:** to evaluate the demographic and clinical profile of occupational cases of sensitization to isothiazolinones in the city of Rio de Janeiro and to describe the presence of these preservatives in national paints. **Methods:** cross-sectional study based on information from medical records of workers who underwent patch testing between 2013-2017. The prevalence of clinical, demographic and occupational characteristics was described and an unadjusted model was used to investigate the association between variables. We sought the presence and concentration of isothiazolinones in the chemical composition sheets of national paints. **Results:** among the 768 workers submitted to the tests, 68 had occupational dermatosis with a positive result for sensitization to methylisothiazolinone/Kathon CG. The most affected occupations were those related to domestic activities and cleaning. There was a greater likelihood of sensitization to isothiazolinones in women and in those with involvement of the hands and legs. Among the 61 paints evaluated, 26 had some isothiazolinone, with methylchloroisothiazolinone being the most common. **Conclusions:** sensitization to isothiazolinones can impact workers' health and demands greater vigilance on cleaning materials and cosmetics, as well as discussing the composition regulation of the paints sold in Brazil.

**Keywords:** occupational dermatitis; allergic contact dermatitis; exposure to chemicals; cross-sectional studies; occupational health.

### Resumo

**Introdução:** a metilisotiazolinona isolada ou associada à metilcloroisotiazolinona (Kathon CG) é um conservante relacionado à dermatite de contato alérgica ocupacional. **Objetivos:** avaliar o perfil demográfico e clínico dos casos ocupacionais de sensibilização a isotiazolinonas no município do Rio de Janeiro e descrever a presença desses preservativos em tintas nacionais. **Métodos:** estudo transversal baseado em informações de prontuários de trabalhadores submetidos a testes de contato entre 2013-2017. **Descreveu-se a prevalência de características clínicas, demográficas e ocupacionais e utilizou-se um modelo não-ajustado para investigar a associação entre variáveis. Buscou-se a presença e a concentração de isotiazolinonas nas fichas de composição química de tintas nacionais. Resultados:** dentre os 768 trabalhadores submetidos aos testes, 68 apresentavam dermatose ocupacional com resultado positivo para sensibilização à metilisotiazolinona/Kathon CG. As profissões mais acometidas foram as relacionadas a atividades domésticas e limpeza. Houve maior chance de sensibilização às isotiazolinonas nas mulheres e naqueles com acometimento das mãos e das pernas. Entre as 61 tintas avaliadas, 26 possuíam alguma isotiazolinona, sendo a metilcloroisotiazolinona a mais comum. **Conclusões:** a sensibilização às isotiazolinonas pode impactar a saúde do trabalhador e demanda maior vigilância com materiais de limpeza e cosméticos, assim como a discussão da regulação da composição de tintas comercializadas no país.

**Palavras-chave:** dermatite ocupacional; dermatite alérgica de contato; exposição a produtos químicos; estudos transversais; saúde do trabalhador.

## Introduction

Isothiazolinones make up a family of preservatives with broad biocidal action, making them used in cosmetics, cleaning materials, paints and various products for industrial use<sup>1</sup>. Among the most used are methylisothiazolinone (MI; CAS 2682-20-4) and methylchloroisothiazolinone (MCI; CAS 26172-55-4), as well as the mixture of both, which is called Kathon CG. Other isothiazolinones such as benzisothiazolinone (BIT; CAS 2634-33-5) and octylisothiazolinone (OIT; CAS 26530-20-1), despite not being commonly used in cosmetics, are preservatives used in household cleaning products, paints and water-based industrial metal fluids<sup>2-4</sup>. More recently, dichloroethylisothiazolinone (DCOIT; CAS 64359-81-5), butylbenzisothiazolinone (BBIT, CAS 4299-07-4) and methylbenzisothiazolinone (MBIT; CAS 2527-66-4) were introduced in the industry, with some reports of sensitization to these substances. However, there are no epidemiological studies<sup>1</sup> yet.

The first occupational case of allergic contact dermatitis (ACD) associated with an isothiazolinone was described in 1960. At the time, workers handling a polyacrylate emulsion for paints and waxes in a factory in Sweden developed eczema after BIT sensitization<sup>1</sup>. Since then, the sensitizing potential of this family of preservatives has been observed in the ACD epidemic to Kathon CG, in the 1980s, and in the current worldwide epidemic of sensitization to MI<sup>5</sup>. Increase in the number of positive patch tests for MI has been noticed especially since 2010. European countries have showed an increase in the prevalence of sensitization to MI between 1.7% and 5.75%, and, in Portugal, the percentage of positive tests for MI jumped from 5.15% in 2012 to 10.9% in 2013<sup>5</sup>. Although current cases of allergy to MI have been attributed to contact with cosmetics, the first report of ACD related to this substance, in 2004, was of occupational nature, affecting a Swedish worker who handled wallpaper glue<sup>1</sup>. Several cases have also been related to exposure to preservatives found in cleaning materials, paints and other industrial products<sup>4,6</sup>.

In the current ACD epidemic caused by exposure to MI, the most affected professions in the epidemiological surveys are painters and other activities related to paints, machine operators and professionals who deal with cosmetics<sup>4</sup>. It is noteworthy that cases of occupational skin diseases associated with sensitization to isothiazolinones

continue to increase in Europe, despite the decline in the occurrence of non-occupational reports from 2014 onwards<sup>1</sup>. Part of this situation is explained by the presence of high concentrations of isothiazolinones in water-based paints and the absence of a regulation in the sector, contrary to what has happened with cosmetics in recent years. It is also known that paints behave like aerosols, so that their components can remain suspended in the environment for weeks, which increases the risk of sensitization in workers involved in the civil construction and paint industry<sup>1,7</sup>.

In Brazil, there has not been yet an epidemiological survey to assess the sensitization profile in the general population and in occupational dermatitis cases, despite the fact that isothiazolinones have been observed in high concentration, especially in cosmetics, cleaning products and paints. Current legislation establishes a concentration of 100 ppm for MI in cosmetics, while Kathon CG is tolerated up to 15 ppm in this type of product, much higher concentrations than those currently used in cosmetics sold in the European continent<sup>8</sup>.

Still in the occupational sphere, the nature of the most appropriate equipment for the protection and prevention of sensitization to MI/Kathon CG is discussed. Hands are frequently affected by these preservatives in reports of ACD and in cases of occupational dermatitis in general, and it is pertinent to assess the most suitable types of gloves for workers who handle products containing these isothiazolinones<sup>9,10</sup>.

The objective of this study was to evaluate the demographic and clinical profile of workers with MI/Kathon CG-associated occupational allergic contact dermatitis in Rio de Janeiro and the occupational impact of sensitization caused by this compound on work activities. The Material Safety Data Sheet (MSDS) [*Ficha de Informação de Segurança de Produtos Químicos (FISPQ)*] of paints sold in the country was also analyzed regarding the presence of isothiazolinones, as well as the national legislation on the use of preservatives in these products.

## Methods

A cross-sectional analytical observational study was carried out from January 2013 to December 2017, in the city of Rio de Janeiro, Brazil.

Data were obtained from the medical records of patients undergoing patch testing at a work-related dermatology service and at an allergic dermatosis outpatient clinic. The first receives users of the Brazilian Unified Health System (*Sistema Único de Saúde* - SUS) over 18 years of age to investigate dermatoses in terms of the occupational nexus. The second is in a philanthropic hospital, which receives users of private health services and the SUS, without age restriction. All workers undergoing patch testing in the period were included.

The epicutaneous test was performed with the Brazilian standard battery of 30 substances (FDA Allergenic Asac Pharma), which contains Kathon CG at 0.5% in petrolatum. MI at 0.2% in aqueous medium was only tested from May 2016, in both institutions. There is an indication to perform the test separately from the MI, as it is found in low concentration in the Kathon CG mixture. So, individuals sensitized to the substance have a negative test when only the mixture is tested<sup>11,12</sup>. The test was applied preferably on the back, using *Finn Chambers*® on the sponsor tape, and the readings were performed at 48 and 96 hours. The gradation proposed by the International Study Group on Contact Dermatitis was used, namely: + = papule and erythema; ++ = vesicles, papule and erythema; +++ = multiple vesicles or blister or ulceration; RI = irritant; negative = absence of skin changes<sup>13</sup>.

The variables studied were: age (in years), sex (male, female), race/color (white, brown, black), professional activity (cook, bricklayer/maid, cleaning, among others), history of personal atopy or atopic dermatitis (yes, no), location of the lesions (hands, feet, face, among others), persistence of lesions on the hands after six months of diagnosis (yes, no), time of the symptoms evolution (in months), use of personal protective equipment (PPE) (regular, irregular, not used), the used gloves material (rubber, vinyl, nitrile, cloth, plastic, others), absence from work activities (in days), professional rehabilitation (yes, no), Brazilian standard battery allergens and additional tests.

Data were tabulated and analyzed using the SPSS 17.0 program (SPSS Inc. Chicago, USA). For occupational cases, the prevalence of positive tests for Kathon CG and MI was described, in addition to the most frequently affected professions. The MOAHLFA index (male, occupational dermatitis, atopic dermatitis, hand dermatitis,

leg dermatitis, face dermatitis, age > 40) was used to describe clinical and demographic characteristics in the sample<sup>14</sup>.

For the cases of sensitization to MI/Kathon CG and those of occupational origin, in addition to the demographic variables, the lesions location, final diagnosis, co-sensitizers, use and type of PPE, absence from work and the need for professional readaptation were described. The analysis of the association between some of these variables and the chance of sensitization to isothiazolinones was performed using Pearson's chi-square test or Fisher's exact test, adopting a statistical significance level of 5%. Odds ratios and 95% confidence intervals were calculated on an unadjusted model for the occurrence of occupational dermatosis caused by MI/Kathon CG, sex, location of lesions, personal history of atopy, age over forty years, work activity, absence from work and professional readaptation, in addition to the presence of chronic hand eczema and the use of PPE.

We also carried out an analysis of the MSDS (*FISPQ*) of wall paints sold in the national market, produced by five different companies, namely: Coral®, Luxens®, Sherwin-Williams®, Suvinil®, Eucatex® and Renner®. The companies were chosen from searches carried out on online paint stores websites, and the MSDS (*FISPQ*) were obtained from the brands' official websites. Information on the presence of isothiazolinone and the concentration used were sought in the sheets.

The research was previously approved by the Research Ethics Committee (CEP) of the Escola Nacional de Saúde Pública Sérgio Arouca, Fiocruz/RJ, under number CAAE 12783519.2.0000.5240, on June 3, 2019. Waiver of signing the Free Informed Consent Form was authorized by the CEP.

## Results

During the study period, 768 individuals underwent the patch test, and 217 (28.3%) of them were diagnosed with occupational dermatosis. **Table 1** shows the most prevalent occupations among all individuals submitted to the patch test, as well as the prevalence of positive tests for isothiazolinones, and demographic and clinical characteristics according to the MOAHLFA index.

**Table 1** Distribution of workers who underwent patch testing, according to positive test results for methylisothiazolinone/Kathon CG and MOAHLFA\* index among those sensitized to isothiazolinones, seen at a work-related dermatology service and at an allergic dermatosis outpatient clinic in Rio de Janeiro (RJ), in the period 2013-2017

Profession	Total of patch tests	Positive tests for MI/Kathon CG	M	O	A	H	L	F	A
	n	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dressmaker/tailor	15	5 (33.3)	-	-	-	5 (100.0)	3 (60.0)	2 (40.0)	5 (100.0)
Clerk/salesperson	51	15 (29.4)	1 (6.7)	3 (20.0)	1 (6.7)	9 (60.0)	3 (20.0)	4 (26.7)	4 (26.7)
Paints/graphics related	15	3 (20.0)	3 (100.0)	3 (100.0)	1 (33.3)	3 (100.0)	2 (66.7)	-	2 (66.7)
Cook	38	8 (21.1)	-	3 (37.5)	1 (12.5)	2 (25.0)	1 (12.5)	3 (37.5)	6 (75.0)
Manicure	12	2 (16.7)	-	2 (100.0)	-	1 (50.0)	1 (50.0)	1 (50.0)	2 (100.0)
Mechanic/metallurgist	20	5 (25.0)	5 (100.0)	2 (40.0)	-	2 (40.0)	4 (80.0)	3 (60.0)	4 (80.0)
Bricklayer/servant	48	3 (6.2)	3 (100.0)	2 (66.7)	-	1 (33.3)	3 (100.0)	-	3 (100.0)
Chemist	14	7 (50.0)	-	1 (14.3)	-	6 (85.7)	3 (42.9)	2 (28.6)	2 (28.6)
Cleaning-related	102	21 (20.6)	4 (19.0)	21 (100.0)	1 (0.5)	15 (71.4)	11 (52.4)	3 (14.3)	11 (52.4)
Hair stylist	8	3 (37.5)	-	2 (66.7)	-	2 (66.7)	1 (33.3)	1 (33.3)	3 (100.0)
Health worker	30	9 (30.0)	1 (11.1)	2 (22.2)	1 (11.1)	5 (55.6)	3 (33.3)	1 (11.1)	6 (66.7)
Office worker	51	13 (25.5)	4 (30.8)	0 (0.0)	1 (7.7)	6 (46.2)	7 (53.8)	4 (30.8)	7 (53.8)
Domestic activities	148	42 (28.4)	-	21 (50.0)	2 (4.8)	30 (71.4)	20 (47.6)	11 (26.2)	32 (76.2)
Driver	16	1 (6.2)	1 (100.0)	-	-	-	1 (100.0)	-	1 (100.0)
Elderly/Child Caregiver	14	5 (35.7)	-	3 (60.0)	1 (20.0)	3 (60.0)	2 (40.0)	2 (40.0)	4 (80.0)
Teacher/education assistant	15	4 (26.7)	-	-	2 (50.0)	2 (50.0)	1 (25.0)	3 (75.0)	2 (50.0)
Doorman	8	2 (25.0)	2 (100.0)	-	-	2 (100.0)	-	-	1 (50.0)
Total	605	148 (24.5)	24 (16.2)	65 (43.9)	11 (7.4)	94 (63.5)	66 (44.6)	40 (27.0)	95 (64.2)

\* MOAHLFA index for description of clinical and demographic characteristics: M: male; O: occupational; A: atopic dermatitis; H: hand dermatitis; L: leg dermatitis; F: face dermatitis; A: age > 40. MI: methylisothiazolinone.

Source: Developed by the authors based on information from the database of patients undergoing patch testing between 2013-2017.

Among occupational cases, patch testing was positive for Kathon CG in 63 subjects, while 28 of 30 MI sensitization tests were positive. Current clinical relevance for Kathon CG was observed in 63 cases and for MI in 27. Thus, considering the occurrence of co-sensitization to MI and Kathon CG, it was possible to establish an occupational nexus in 68 individuals sensitized to some isothiazolinone.

In the sample of individuals with occupational dermatosis triggered by isothiazolinones (n = 68), 33 workers came from the work-related dermatology service, while 35 came from the allergic dermatoses outpatient clinic. There was a predominance of females (n = 57), of black skin color/race (n = 30), and the mean age was 45.5 years (standard deviation = 10.2 years). There was a statistically

significant association between occupational dermatosis caused by MI/Kathon CG and female sex (OR: 4.24; 95%CI: 2.06; 8.71;  $p < 0.01$ ), involvement of the hands (OR: 3.73; 95%CI: 2.1; 6.7;  $p < 0.01$ ) and lower limbs (OR: 3.19; 95% CI: 1.72; 5.93,  $p < 0.01$ ). The analysis of the association with facial involvement ( $p = 0.59$ ), atopic dermatitis ( $p = 0.69$ ) and age over 40 years ( $p = 0.53$ ) did not show statistical significance. The most prevalent professions were those related to domestic activities (n = 21) and cleaning (n = 21). With regard to activities involving contact with paint, only two cases were observed in bricklayers/servants and three in the group of professions related to paints, with activities in the chemical industry and with printing activities (Table 1). However, the only occupation

that showed a greater likelihood of sensitization by MI/Kathon CG, with statistical significance, was related to domestic activities (OR: 4.31; 95%CI: 2.03; 9.15;  $p < 0.01$ ) (**Table 2**).

Regarding injury location, there was a predominance of eczema on the palms ( $n = 36$ ), the

extensor surface of the upper limbs ( $n = 35$ ), the back of the hands ( $n = 33$ ) and the extensor surface of the lower limbs ( $n = 27$ ) (**Table 3**). In individuals with hand involvement, even with instructions to avoid contact with isothiazolinones, 39 had lesions in this location after six months.

**Table 2** Association between professions and sensitization to methylisothiazolinone/ Kathon CG among workers with occupational dermatosis treated at a work-related dermatology service and at an allergic dermatosis outpatient clinic in Rio de Janeiro (RJ), in the period 2013-2017

Profession	Total occupational	Total positive tests for MI/Kathon	OR	95%CI	p-value
	n	n (%)			
Domestic activities	35	21	4.31	2.03 - 9.15	< 0.01*
Cleaning-related	60	21	1.26	0.67 - 2.37	0.47*
Paints-related	15	3	0.94	0.24 - 3.74	0.93**
Elderly/Child Caregiver	6	3	2.25	0.44 - 11.43	0.38**
Clerk/salesperson	6	3	2.25	0.44 - 11.43	0.38**
Chef	19	3	0.38	0.11 - 1.36	0.19**

MI: methylisothiazolinone; OR: odds ratio; CI: confidence interval.

\*Chi-square test; \*\*Fisher's exact test.

Source: Developed by the authors based on information from the database of workers submitted to the patch test between 2013-2017.

**Table 3** Location of injury in workers with allergic contact dermatitis caused by isothiazolinones and occupational nexus, treated at a work-related dermatology service and at an allergic dermatosis outpatient clinic, in Rio de Janeiro (RJ), in the period 2013-2017

Location of injuries	n
Cephalic	
Scalp	4
BTE	1
Ear pavilion	7
Face	11
Eyelids/periorbital	5
Labial/perioral	2
Neck	11
Trunk	
Anterior thorax	10
Mammary areola	5
Armpits	5
Back	11
Abdomen	16
Limbs	
UL extensor face	35
LL flexor face	10
Dorsum of hands	33
Palms	36
Interdigital space of hands	6
Fists	5
LL extensor face	27
LL flexor face	18
Dorsum of feet	20
Soles	9
Interdigital space of feet	-

BTE: behind the ears; UL: upper limbs; LL: lower limbs.

Source: Developed by the authors based on information from the database of patients undergoing patch testing between 2013-2017.

The most prevalent co-sensitizations were those related to nickel sulfate (n = 21), perfume-mix (n = 13), carba-mix (n = 11), thimerosal (n = 11), cobalt chloride (n = 11) and thiuram-mix (n = 10). Positive tests for thimerosal were not clinically relevant.

There was a final diagnosis of ACD associated with cosmetics in 16 subjects, with cleaning product in 10, with cosmetics and cleaning products in 38, and with paints in 4. The median duration of symptoms before diagnosis was 12 months (interquartile range: 9-36).

The regular use of personal protective equipment (PPE) was mentioned by 39 individuals and irregularly by 11, while 14 did not use PPE. Considering the type of gloves, there was a predominance of rubber (n = 40), and other materials such as nitrile (n = 2), vinyl (n = 2), cloth (n = 2) and plastic (n = 1) were also mentioned. There was no statistically significant association between chronic hand eczema and the use of PPE (OR: 0.53; 95%CI: 0.09; 2.92; p = 0.46).

Leave of absence from work was observed in 26 cases, with a median absence from work of 120 days (interquartile range: 60-435). Professional readaptation was necessary in 12 cases. Among occupational cases, there was no association between sensitization to isothiazolinones and absence from work (OR: 1.07; 95%CI: 0.59; 1.94; p = 0.83), professional readaptation (OR: 1.99; 95%CI: 0.87; 4.54; p = 0.09), or hand involvement (OR: 0.99; 95%CI: 0.51; 1.96; p = 0.99).

The analysis of MSDS (FISPQ) of 61 paints sold in the national market regarding the presence of isothiazolinones showed that 35 did not refer to the presence of these preservatives, 13 had MI in a concentration of up to 3,000 ppm, 16 had MCI in a concentration of up to 3,000 ppm, 7 had the mixture of MCI and MI up to 1000 ppm, 12 contained OIT up to 10<sup>4</sup> ppm and 1 (1.64%) reported the presence of DCOIT up to 3000 ppm. BIT was present in an ink, but the concentration was not specified (Table 4).

**Table 4** Analysis of Material Safety Data Sheet (MSDS) [Ficha de Informação de Segurança de Produtos Químicos (FISPQ)] for paints sold in Brazil regarding the presence of any isothiazolinone and its concentration (n = 61)

		Coral® n = 10	Luxens® n = 11	Sherwin-Williams® n = 10	Suvini® n = 10	Eucatex® n = 9	Renner® n = 11
MI	≤ 0.1	-	-	6	-	-	-
	0.1-0.3	-	-	-	-	7	-
MCI	≤ 0.1	3	-	6	-	-	-
	0.1-0.3	-	-	-	-	7	-
MCI/MI	< 0.1	-	-	-	7	-	-
BIT	a	-	-	-	1	-	-
OIT	< 1	3	-	-	-	-	-
	0.05-0.1	-	-	1	-	-	-
	0.1-0.3	-	-	-	-	7	-
	a	-	-	-	1	-	-
DCOIT	≤ 0.3	-	-	1	-	-	-

MI: methylisothiazolinone; MCI: methylchloroisothiazolinone; BIT: benzisothiazolinone; OIT: octylisothiazolinone; DCOIT: dichloroethylisothiazolinone; a: presence of isothiazolinone, but without concentration information.  
Source: Material Safety Data Sheet.

## Discussion

Epidemiological surveys on the epidemic of sensitization to MI/Kathon CG preservatives in other countries have already demonstrated the association of this condition with occupational exposure, female sex and hand involvement, as observed in this study,

in which association with lower limb involvement was also found<sup>4</sup>. In this study, we observed that the professions that were most affected by ACD associated with MI/Kathon CG were domestic activities and cleaning, occupations that have regular contact with cosmetics and hygiene products, known sources of exposure to isothiazolinones. In addition,

the observed demographic profile is justified by the fact that these are activities usually carried out by women and, due to Brazilian social issues, by black and brown people.

In the sample studied, ACD cases were not as prevalent among professions that have contact with paints, unlike what was observed in studies carried out in other countries. Furthermore, no association with isothiazolinone allergy was found, possibly due to the small number of cases. A European study carried out between 2009 and 2012 demonstrated the association between MI sensitization and the occurrence of occupational dermatitis, especially among painters and beauticians<sup>15</sup>. A multicenter study carried out in the same period in Denmark showed an association of MI sensitization with machine operators, painters and construction workers (roof and brick handling), while Kathon CG sensitization was associated with painters, workers who handle cosmetics, machine operators and welders<sup>4</sup>. These differences in the profile of professions are expected according to the population group and the economic activities carried out in the region studied, especially in a heterogeneous country with the dimensions of Brazil<sup>10</sup>. It is known that occupations related to domestic activities are not so common in high-income countries and therefore they are not expected to appear in European statistics of occupational allergy to isothiazolinones cases.

The most prevalent co-sensitizers observed are also present in cleaning products and cosmetics such as perfume-mix. Co-sensitization caused by MI in association with fragrances had already been reported<sup>16</sup>. The rubber additives, carba-mix and thiuram-mix, frequently used in PPE such as gloves and boots, appear as common co-sensitizers, probably due to the presence of occupational cases in the sample.

Chronic hand eczema from occupational ACD is often more prevalent among those who do not use PPE or do so irregularly. The repeated contact with rinse-off cosmetics and cleaning products, which occurs in some professions, and without the use of gloves, makes them relevant agents of occupational contact dermatitis on the hands<sup>15</sup>. A point to be considered is the high concentration of MI in cleaning products, such as detergents, which is often not reported on the labels<sup>17</sup> and contributes to the chronic hand eczema frequently observed in professions related to domestic activities and cleaning, as verified in this study. Household detergents contain different isothiazolinones in high concentrations, such as MI present in up to 200 ppm, which, in addition to causing chronic hand eczema, can behave like aerosols when applied to large surfaces or used as spray<sup>2</sup>.

One way to prevent chronic hand eczema among sensitized people is wearing gloves regularly. In this study, more than half of the sample mentioned the regular use of these protective equipment, which often occurs after the onset of the chronic inflammatory process in the hands and not as a means of prevention. Maor and Nixon reported that among cooling tower workers sensitized to Kathon CG, 47% did not wear gloves and 53% wore them inappropriately<sup>18</sup>. In this sense, searching for the most suitable material for the manipulation of isothiazolinones, Espasandin-Arias and Goossens demonstrated, through a patch test fixed for 48 hours on the back of a sensitized patient, that MI is able to penetrate through rubber gloves. Although the test conditions often do not reflect the reality of the work process, it did demonstrate that MI is not able to penetrate through nitrile gloves<sup>19</sup>. Thus, current recommendations are for preference to be given to reusable nitrile gloves above the elbows, as a way of preventing MI/Kathon CG sensitization, especially among industrial workers<sup>1,18</sup>. Attention should also be given to the composition of gloves, since BIT has already been found in polyvinyl (PVC) gloves, causing ACD in such health professionals as doctors and dentists<sup>20</sup>.

The absence from work activities represents the impact of occupational dermatoses in the productive sphere and was observed in 38.2% of the studied sample sensitized to isothiazolinones. Although the prevalence of sick leave did not differ from other causes of occupational skin diseases, it was higher than that observed in a study carried out in the United States, which showed that this indicator, between the years 1972-1997, ranged from 12.6 to 25%<sup>21</sup>. The analysis of the compulsory notification forms of occupational dermatoses in Brazil registered between 2007-2014 showed absence in 29% of cases<sup>22</sup>. The number of days off work can be used to assess the the clinical condition severity, although difficulties in establishing the occupational dermatitis diagnosis and access to health services also influence the index by favoring the progression of the disease. The annual American study conducted in 1997 by the US Bureau of Labor Statistics showed an average absence of three days due to occupational dermatoses, a number well below the median of 120 days observed in this Brazilian study with MI/Kathon CG<sup>21</sup>.

The high occupational ACD occurrence associated with isothiazolinones in Europe is partly explained by the lack of a legislation that limits the use of MI, mainly in paints and cleaning products<sup>2,23</sup>. On the European continent, it is not mandatory to provide the chemical composition specification on labels of paints and glues that follow

the concentrations of isothiazolinones below: MCI/MI < 15 ppm; MI < 300 ppm; and BIT < 360 ppm. As for biocides for industrial use, the concentration of MI, MCI and BIT can be greater than 5,000 ppm<sup>2</sup>. In Brazil, paints are not subject to registration and are not regulated by government agencies such as the *Agência Nacional de Vigilância Sanitária* (Anvisa), as is the case with cosmetics. In the context of an ACD epidemic associated with MI/Kathon CG, this may represent a risk, especially in the occupational sphere, given the high concentrations of several isothiazolinones in national paints, as verified in the assessed MSDSs. Analyses of the chemical composition of paints in Denmark found MI, OIT and BIT isothiazolinones, although the industry reported that their products contained only the first substance<sup>24,25</sup>. Lundov et al.<sup>7</sup> analyzed 19 brands of water-based paints by means of liquid chromatography combined with mass spectrometry and observed the presence of MI in all samples at a concentration of 10-300 ppm, of BIT in 16 brands at a concentration of 1.5-360 ppm, and of MCI in 4 paints at a concentration of 2-14 ppm. The authors also evaluated the capacity of isothiazolinone emission from these paints and described that in the laboratory, after applying two layers of paint to a wall, MI was released continuously for up to 42 days, while BIT was detected only in low concentration<sup>7</sup>. This experiment reflects the risk to which construction workers, such as painters or bricklayers, are exposed in the work environment for over several days. It is estimated that a patient with MI sensitization needs to stay away for at least 5.5 weeks from a place recently covered with paints containing the substance<sup>26</sup>. Thus, the preference should be for the use of paints without isothiazolinones, although these are more expensive and difficult to find. Other options for neutralizing isothiazolinones in recently painted environments

are alkalization or the addition of sulfites, which can be done in order to reduce the sensitizing potential. However, considerations must be made regarding the risk of burns caused by alkalization or of sensitization produced by the sulfite itself. Another possibility would be to use 2% glutathione creams on painted walls. This antioxidant breaks the aromatic ring of isothiazolinones, allowing the worker to remain in newly painted environments. As a general measure, ventilation optimization is also adopted in the place where the paint was applied<sup>2,27-29</sup>.

The limitations of this study are the small sample size, which in some cases made the analysis of statistical associations unfeasible, and the incomplete performance of the MI patch test, which may have led to the loss of some cases. Another issue is the evaluation of paint composition, which was restricted to reading the MSDS (*FISPQ*), and that chemical analyses of products samples were not carried out.

## Conclusion

The current ACD epidemic associated with MI, even with the little data on this available in the country, seems to have the potential to impact the workers' health in Brazil. In this study, the most affected professions differ from those observed in other countries, which may indicate the need for greater vigilance not only regarding the composition of paints, but also of cleaning materials and cosmetics sold in the Brazilian market. Several isothiazolinones in high concentrations were found in approximately half of the paints MSDS (*FISPQ*) sample evaluated, representing a potential risk for certain professions, what should motivate the discussion about the need for a specific legislation on the subject in Brazil.

## Authors' contributions

Villarinho ALCF contributed to study design, data collection, analysis and interpretation, article preparation and critical review. Melo MGM contributed to data collection, analysis and interpretation, article preparation, and critical review. Moutinho WCD contributed to study design, article preparation and critical review. Teixeira LR contributed to data collection, analysis and interpretation, article preparation and critical review. All of the authors approved the final version and take full responsibility for the published article.

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