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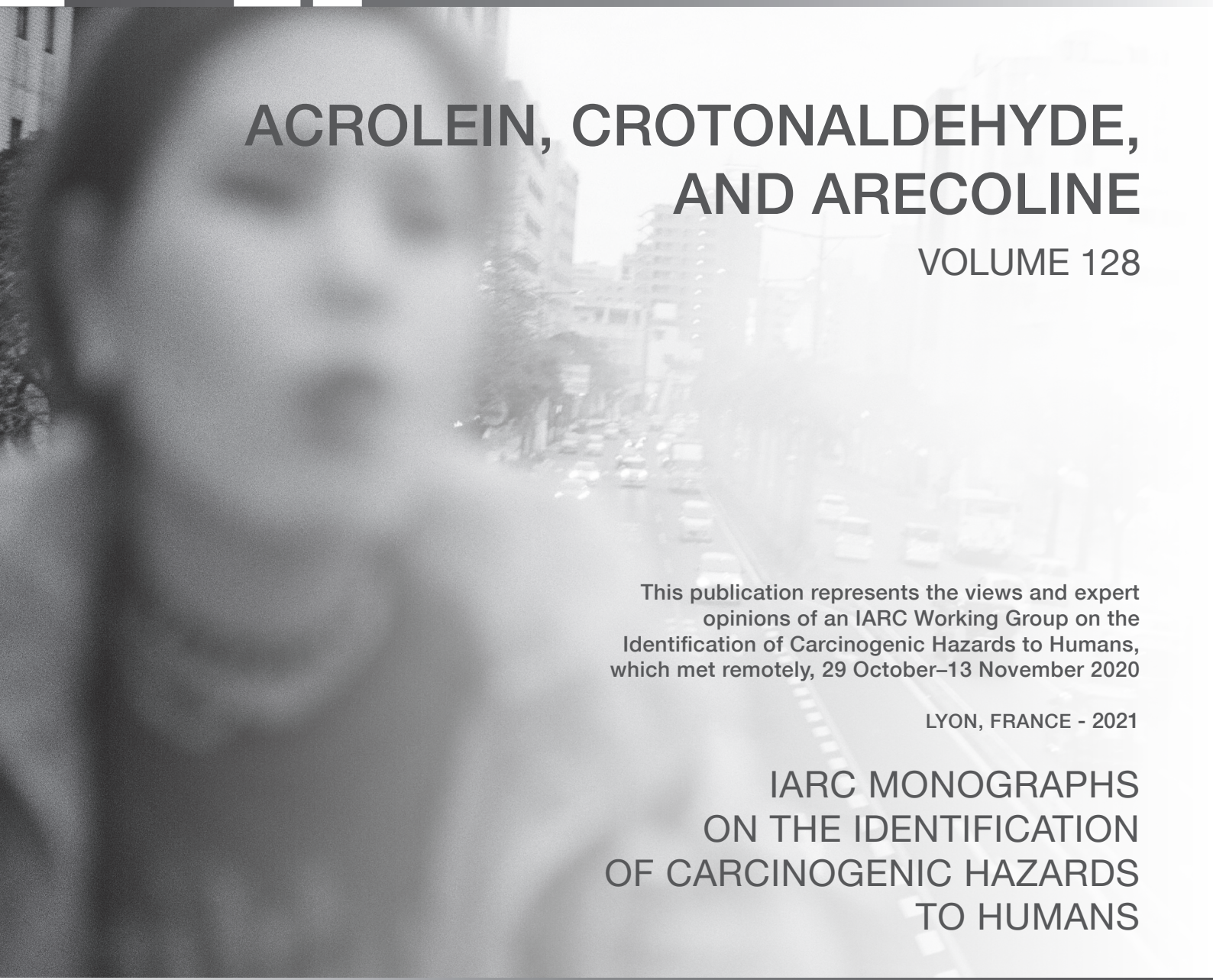

ACROLEIN, CROTONALDEHYDE, AND ARECOLINE

VOLUME 128

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IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS

International Agency for Research on Cancer

World Health Organization

Table S1.5 Exposure assessment review and critique for mechanistic studies in humans exposed to acrolein

Reference and outcome	What was the study design?	What methods were used for the exposure assessment?	What was the definition of external exposure?	Was endogenous exposure defined?	Was the exposure defined well?	What route of exposure was assessed?	How was the intensity of exposure assessed?	How was the duration of exposure assessed?	Was cumulative exposure assessed?	Was exposure assessed before outcome being ascertained?	What was the timing of exposure relative to the outcome?	Was there known exposure to any other carcinogens?
McDiarmid et al. (1991) Acrolein−DNA adducts	Analytical study in 27 cancer patients versus untreated control group (*n* = 15)	CP treatment	CP dose (acrolein is a principal metabolite of CP)	No	Moderately well-defined (controls for smoking, but not other exposures)	Oral	Lifetime and last month dose	Lifetime and last month use of CP	No	No	NA	Yes, tobacco smoke toxicants
Nath et al. (1998) Acrolein−DNA adducts	Cross-sectional study. DNA from gingival tissues from 11 non-smokers and 12 smokers analysed for acrolein and crotonaldehyde adducts	^{32}P-Postlabelling for DNA adducts of crotonaldehyde and acrolein	Smokers and non-smokers	Levels in non-smokers	Self-reports, no chemical confirmation of smoking status	Inhalation assumed	Adduct levels and self-reports. No analysis of this data was provided	None	Adducts should accumulate based on the cell lifespan and repair	Adduct levels were outcome	NA	Tobacco smoke
Lee et al. (2014) Acrolein−DNA adducts	Analytical study in normal urothelial mucosa (*n* = 19) and bladder tumour tissue samples (*n* = 10)	Measurement of Acrolein−DNA adducts	No external exposure defined	No endogenous exposure defined	No definition of exposure. Exposure was based on Acrolein−DNA adducts only	Not specified	Intensity of exposure was assessed using a one-off sample	No external exposure was considered, hence no duration of exposure	No	No	Unclear. Possible endogenous accumulation due to disease. It was not clear whether the exposure is a cause or a result of the bladder tumours	NR
Zhang et al. (2007) Acrolein−DNA adducts	Analytical study in lung tissue samples of current and ex-smokers (*n* = 30)	Measurement of acrolein−DNA adducts	Self-reported smoking history with current smoking confirmed by urinary biomarkers cotinine and nicotine	No endogenous exposure defined	Moderately well defined (history of smoking, but not other exposures; acrolein−DNA adducts measurement)	Inhalation	Current and ex-smoking combined with intensity of exposure assessed using a one-off sample	No, based on self-reports of smoking history	No	No	Exposure preceded outcome	Yes, tobacco smoke toxicants
Chen & Lin (2011) Acrolein−DNA adducts	Cross-sectional study of salivary DNA adduct levels in 27 volunteers. Demonstration study	Salivary DNA adducts for acrolein and crotonaldehyde (among others)	None	No		None	Adduct levels by individuals	NA	No	No outcome assessed	NA	Yes, 8 adducts were measured
Al-Rawithi et al. (1998) Urinary excretion and pharmacokinetics of acrolein	Analytical study in bone-marrow transplant patients receiving CP (*n* = 16)	CP treatment	CP dose (acrolein is a principal metabolite of CP)	Endogenous exposure not considered	No, external exposure not considered	i.v.	CP dose	Total CP dose during treatment period	No	No	Exposure preceded outcome	No
Takamoto et al. (2004) Urinary excretion of acrolein	Analytical study in patients receiving CP and IP(*n* = 19)	CP and IP treatment	CP/IP dose (acrolein is a principal metabolite of CP and IP)	Endogenous exposure not considered	No, external exposure not considered	i.v.	CP/IP dose	Total dose during treatment period	No	No	Exposure preceded outcome	No
Wang et al. (2019) Detoxification metabolites	Analytical study in consumers of fried foods (*n* = 19)	Measurement of acrolein−DNA in buccal cells and urinary acrolein metabolites	One meal of fried foods from three commercial fast food restaurants	No	No. No specific data about food consumption reported, including no data on acrolein content of foods. Non smoking participants only	Oral	One single meal of fast food	Duration not considered in study (single exposure study)	No	Unclear. Food intake not reported	Exposure preceded outcome	No
Ruenz et al. (2019) Detoxification metabolites	Duplicate diet studies (a) in non-smoking volunteers under defined	Measurement of urinary metabolites	Different phases of controlled diet with or without heat-	Background exposure assumed as being	Yes. Consideration of all known external acrolein exposures	Oral	Controlled diet of heat processed foods	Two phases of heat-processed food consumption	Total diet exposure, smoking and	Yes	Exposure preceded outcome	No

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	living conditions (n = 14); and (b) in non-smoking volunteers on unrestricted (n = 10) or vegan diet (n = 10) under free living conditions		processed food items. Questionnaires about potential sources of non-dietary exposure such as open fire, tobacco smoke. Smoking status confirmed by tobacco biomarkers	endogenous, specifically in the group at controlled environment absent of known external exposures				followed by washout periods	environmental exposure excluded			
Yang et al. (2019) Acrolein−DNA adducts	Analytical study in lung DNA of non-smokers (n = 18) and smokers (n = 19)	Measurement of Acrolein−DNA adducts	Self-reported smoking status	No	Moderately well-defined (control for smoking, but not other exposures)	Inhalation	Intensity not assessed	Duration not assessed	No	No	Exposure preceded outcome	Yes, tobacco smoke toxicants
Liu et al. (2005) Acrolein−DNA adducts	Analytical study in brain DNA (n = 13)	Measurement of acrolein−DNA adducts	No external exposure defined	No	No definition of exposure. Exposure was based on acrolein−DNA adducts only	None	Intensity not assessed	Duration not assessed	No	No	No exposure assessment	No
Zhang et al. (2011) Acrolein−DNA adducts	Analytical study in leukocyte DNA from 25 smokers and 25 non-smokers	Measurement of acrolein−DNA adducts	Self-reported smoking status	No	Moderately well-defined (control for smoking, but not other exposures)	Inhalation	Intensity not assessed	Duration not assessed	No	No	Exposure preceded outcome	Yes, tobacco smoke toxicants
Chung et al. (2012) Acrolein−DNA adducts	Analytical study in lung DNA (n = 5)	Measurement of acrolein adducts	No external exposure defined	No	No definition of exposure. Exposure was based on acrolein adducts only	None	Intensity not assessed	Duration not assessed	No	No	No exposure assessment	No
Yin et al. (2013) Acrolein-DNA adducts	Analytical study in leukocytes (n = 5)	Measurement of Acrolein adducts	No external exposure defined	No	No definition of exposure. Exposure was based on Acrolein adducts only	None	Intensity not assessed	Duration not assessed	No	No	No exposure assessment	No
Alamil et al. (2020) Acrolein−DNA adducts	Demonstration study; 2 cross sectional samples analysed. One smoker and one non-smoker: early method validation. Measured acrolein and crotonaldehyde DNA adducts	Smoking status from banked samples No confirmation provided	Smoking status	Non-smoker levels were reported for one person	No. Textual reference to 30 cigarettes per day for the smoker	Inhalation assumed for the smoker	Self reports	DNA adducts measured in lymphocytic DNA. Cells have various life spans. Smoker was a “current” smoker seeking to stop	No. See previous columns.	The measurement was the outcome	The measurement was the outcome	Yes. Tobacco smoker
Nath & Chung (1994) Acrolein−DNA adducts	Demonstration study. Spot samples of human livers DNA (3 people)	^{32}P-Postlabelling for DNA adducts of crotonaldehyde and acrolein	None	None	No exposure was defined	Unknown	Adduct levels, but no quantitation provided	None	Adducts should accumulate until cell division in liver	No outcome assessed	NA	Unknown
Weng et al. (2018) Acrolein−DNA adducts	Analytical study in buccal cells (n = 33 versus n = 17) and lung tissues (n = 41 versus n = 13) of smokers versus non-smokers	Measurement of acrolein−DNA adducts in buccal cells and lung tissues	Self-reported smoking status	No	Moderately well-defined (controls for smoking, but not other exposures)	Inhalation	Intensity not assessed	Duration not assessed	No	No	Exposure preceded outcome	Yes, tobacco smoke toxicants

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Bessette et al. (2009) Acrolein−DNA adducts	Analytical study in buccal cells (n = 6) of tobacco smokers of > 20 cigarettes per day on a noncontrolled diet	Measurement of acrolein−DNA adducts in buccal cells	Self-reported smoking status	No	Moderately well-defined (control for smoking, but not other exposures)	Inhalation	> 20 cigarettes per day	Duration not assessed	No	No	Exposure preceded outcome	Yes, tobacco smoke toxicants
Fu et al. (2018) Acrolein−DNA adducts	Analytical study in liver samples of HCC patients (n = 90 and n = 45)	Measurement of acrolein−DNA adducts in liver samples	None	No	No definition of exposure. Exposure was based on Acrolein adducts only	None	Intensity not assessed	Duration not assessed	No	No	NA	Unknown

CEMA, *N*-acetyl-*S*-(carboxyethyl)-L-cysteine ; CP, cyclophosphamide; HCC, hepatocellular carcinoma; HPMA, *N*-acetyl-*S*-(3-hydroxypropyl)-L-cysteine; i.v., intravenous; IP, ifosphamide; NA, not available.

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