

RESEARCH REVIEW



Zozial of Mizoram: Identity, Chemistry, Exposure and Health Implications of an Indigenous Tobacco Product

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Zozial is an indigenous hand-rolled, non-filter tobacco product of Mizoram, northeast India, prepared from locally cultivated *Nicotiana tabacum* L. (Solanaceae). Despite its long-standing local use, evidence concerning Zozial is distributed across ethnographic/product descriptions, tobacco-plant chemistry, tobacco-specific nitrosamine analysis and epidemiological studies, while several critical exposure steps remain uncharacterized. In this review, the available studies are examined according to the type of evidence they provide: direct studies on Zozial, older studies describing a comparable local product, studies on other combustible tobacco products, and general tobacco toxicology. Published analysis of Mizoram-grown tobacco demonstrates a broad elemental profile and selective accumulation of cadmium, whereas recent isotope-dilution LC-MS/MS analysis directly quantified nitrate, nitrite, tobacco-specific alkaloids and tobacco-specific nitrosamines in Zozial. Case-control studies in Mizoram have reported associations of Zozial, or historically described local cigarette closely matching the product, with lung and stomach cancer. However, filler composition is not equivalent to smoke yield or absorbed dose. Standardized mainstream and sidestream emissions, constituent transfer, Zozial-specific smoking topography, internal exposure and product-specific biomarkers of biological effect remain incompletely characterized in the published literature. Therefore, the comparatively low concentrations of selected tobacco-specific nitrosamines reported in one study, or the presence of potentially toxic elements in the tobacco, are not sufficient to decide whether Zozial is safer or more harmful than manufactured cigarettes. The available evidence is therefore considered along the sequence from cultivation and processing to product composition, combustion, exposure, biological response and disease, with emphasis on the measurements still needed for a reliable exposure and risk assessment.

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mizoacadsci@gmail.com**Keywords :** cadmium, indigenous tobacco, nitrosamines, trace elements, Zozial

Introduction

Tobacco smoking is an established cause of cancer and multiple chronic diseases, and tobacco smoke contains thousands of chemical constituents, including numerous toxic and carcinogenic agents.^{1–3} Yet 'smoked tobacco' is not a chemically uniform exposure. Cultivar, soil chemistry, agronomic practice, curing and storage, tobacco mass, wrapping material, additives, filtration, ventilation, combustion conditions and user puffing behaviour can alter both the unburned product and the smoke delivered to the user.^{4–8} Product-specific characterization is therefore especially important for indigenous and locally manufactured tobacco products.

Mizoram has a particularly high burden of tobacco use and tobacco-associated cancer. Historical surveys documented high tobacco use in the Mizo population,⁹ and more recent cancer-risk-factor surveillance continues to show a high prevalence of tobacco exposure.¹⁰ National cancer-registry analyses have also identified Aizawl/Mizoram among Indian populations with very high incidence of cancers associated with tobacco use.^{11,12,23} These population-level observations provide context, but they cannot be used to attribute Mizoram's cancer burden to any single tobacco product.

Zozial is a locally produced, hand-rolled, non-filter smoking tobacco product prepared from tobacco cultivated in Mizoram. Published chemical work describes mature *Nicotiana tabacum* L. (Solanaceae) leaves being harvested, physically softened, sun-cured during the cooler season, reduced to coarse flakes and rolled by hand in cigarette paper.¹³ The doctoral work from which much of the modern scientific characterization originated also records the product's longstanding cultural and agrarian setting.¹⁴

The scientific literature is complicated by nomenclature. In contemporary Mizo usage, Zozial specifically denotes the indigenous hand-rolled product considered in this review, whereas meizial may be used more broadly for smoking tobacco or cigarettes. Some epidemiological papers used the spelling meiziol for a local cigarette. In Mizo, however, meiziol is not a distinct tobacco term; it is a misspelling of meizial. Phukan *et al.*¹⁵ nevertheless described the product they called meiziol as a locally prepared cigarette rather than relying on the name alone. Accordingly, the spelling meiziol is retained only when reporting those published studies, while equivalence with Zozial is judged from the accompanying product description.

Existing Zozial-related evidence addresses isolated points along an exposure pathway. Epidemiological studies have examined stomach, lung and head-and-neck cancers;^{15–20} elemental analysis has characterized Mizoram-grown tobacco and corresponding soils;¹³ and a 2026 study quantified nitrate, nitrite, tobacco-specific alkaloids (TSAs) and tobacco-specific nitrosamines (TSNAs) in Zozial and other smoking products.²¹ A previous review addressed tobacco and health broadly,²² but did not critically reconstruct Zozial as a distinct product-specific exposure system.

This review examines three related questions: how Zozial should be defined as a tobacco product, which parts of the pathway from cultivation to disease have been studied directly, and where interpretation still depends on evidence from other tobacco products. Keeping these points separate is necessary to avoid either understating or overstating the evidence on Zozial.

Approach to evidence and terminology

Types of evidence

Four evidence classes are used throughout this review. Class I comprises direct Zozial evidence in

Table 1. Published evidence inventory for Zozial and closely related Mizoram evidence. Evidence classes follow Section 2.1. In cited studies, meiziol is retained as printed; throughout this review, it is treated as a misspelling of meizial.

Domain	Terminology	Design	Measurement	Defensible finding	Class	Principal limitation
Product identity / preparation	Zozial	Product characterization	Construction and processing	Indigenous hand-rolled, non-filter product; documented local production pathway	I	Product standardization across producers remains limited
Elemental chemistry	Mizoram-grown tobacco / Zozial source	Analytical study	INAA / AAS; soil-plant analysis	Element-selective uptake and translocation; Cd showed strongest reported leaf bio-concentration	I	Filler concentration is not smoke transfer or inhaled dose
Nitrate / alkaloids / TSNAs	Zozial	29-product analytical study	Isotope-dilution LC-MS/MS	Direct product chemistry; Zozial had the lowest nitrate and total TSNA values within that dataset	I	Does not characterize total smoke toxicity
Stomach cancer	Meiziol (source spelling)	Case-control	Exposure history	Association reported for locally described cigarette	II	Source spelling error; retrospective exposure assessment
Lung cancer	Zozial	Case-control	Exposure history	Association reported for explicitly named Zozial use	I	Observational design; no constituent-specific causation
Head and neck cancer	Zozial mentioned	Case-control	Smoking exposure	Smoking associated with HNSCC; Zozial common among patients	Contextual	Effect estimate is for smoking overall, not Zozial specifically

which the product is explicitly identified and analytically or epidemiologically studied. Class II comprises historical product-equivalent evidence in which another local term is used but the product description closely matches Zoizal. Class III comprises comparative evidence from other combustible tobacco products, such as manufactured cigarettes, roll-your-own cigarettes or bidis; this evidence can establish plausibility or identify measurements that matter, but cannot be transferred quantitatively to Zoizal. Class IV comprises established general tobacco toxicology and mechanistic evidence. This classification is used to make clear when a statement comes from direct Zoizal research and when it is based on evidence from other tobacco products. The published evidence inventory is summarized in Table 1.

Operational definition

For this review, Zoizal is operationally defined as the indigenous Mizoram hand-rolled, non-filter smoking tobacco product prepared from locally cultivated tobacco and traditionally processed tobacco filler. Published work identifies the plant as *N. tabacum* and describes a sequence of priming, physical softening, sun-curing, coarse fragmentation and hand rolling in the production system investigated.¹³ This is an operational scientific definition of the product represented in the available literature, not a legal or commercial standard and not evidence that every producer follows an identical process. The documented product pathway and the terminology used in this review are summarized in Figure 1.

Meizial, Zoizal and the published misspelling meiziol

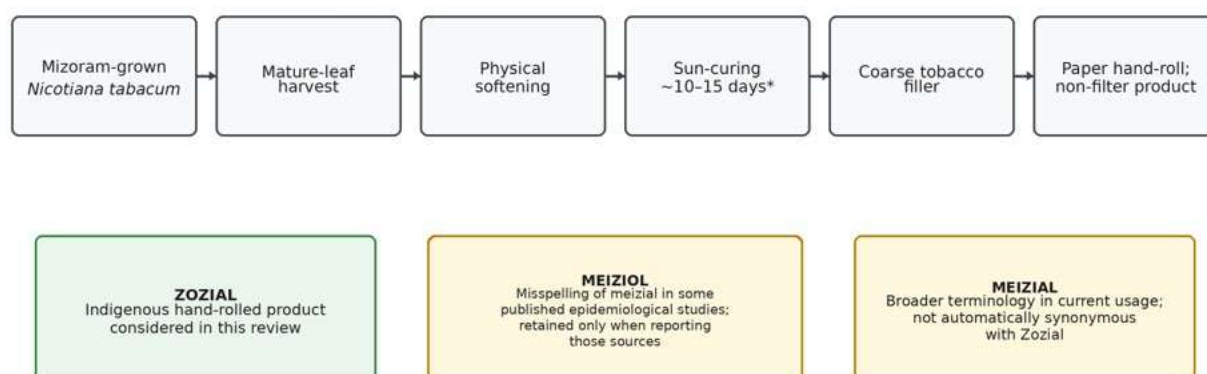
Meizial and Zoizal should be distinguished, while meiziol should not be treated as a third Mizo tobacco term. The thesis used meizial for branded Indian/Myanmar cigarettes and Zoizal for the local handmade cigarette.¹⁴ Older epidemiological papers, however, printed meiziol for a local cigarette.^{15–18} In this review, meiziol is treated as a misspelling of meizial and retained only when reporting the terminology of those sources. Whether an older study describes a product equivalent to Zoizal is therefore judged from the accompanying product description, not from the misspelled term.

From cultivation to Zoizal: a chemically consequential production chain

Published work on Mizoram-grown tobacco describes cultivation principally for preparation of Zoizal and reports that the cultivation sites investigated did not routinely use chemical fertilizers or pesticides.¹³ The original publication uses the description 'organically cultivated'; because 'organic' can imply formal certification, the present review instead describes the reported agricultural practice without implying certification or universality across all Zoizal production.

Processing is chemically relevant. In the production system described by Lalrammawia et al.

Zoizal: product identity and documented production pathway



*Duration shown for the production system reported by Lalrammawia et al. [13]; not asserted as a universal specification.

Figure 1. Zoizal product identity and documented production pathway. The production sequence summarizes the system described in the published Mizoram tobacco study.¹³ Terminological boxes distinguish Zoizal, the published misspelling meiziol and broader meizial usage; product equivalence is judged from description rather than from the misspelled label.

al.¹³, mature leaves were harvested by priming, physically softened, sun-cured for approximately 10–15 days during cooler months until darkening and chlorophyll loss, reduced to coarse flakes and hand-rolled. In tobacco generally, curing and storage alter nitrogen chemistry and can create conditions for nitrosation of tobacco alkaloids; nitrate reduction to nitrite and subsequent nitrosation contribute to formation of NNN and NNK during tobacco processing.²⁴ These are established tobacco-chemistry mechanisms, but their individual contributions during traditional Zoizal processing have not been quantified directly.

The product is non-filtered.^{13,14} That physical fact is important, but the common inference 'no filter = greater exposure' is too simple. Cigarette design and filter ventilation can alter smoke chemistry, constituent transfer and puffing behaviour in manufactured cigarettes.^{4,7,25} Metals also differ in their partitioning and filtration behaviour; cadmium, arsenic and lead do not transfer identically from filler to smoke.^{25,27} These are comparative cigarette data, not Zoizal measurements. Thus the relevant scientific question is what mass of each constituent reaches a Zoizal smoker under realistic use.

Elemental chemistry of Mizoram-grown tobacco

The most substantial direct chemical evidence before the 2026 TSNA study is the multi-element investigation of tobacco plants and corresponding

soils from eight cultivation sites in four districts of Mizoram.¹³ Essential elements and 28 non-essential elements were quantified in leaves, stems, roots and soils using neutron activation analysis and atomic absorption spectrometry. The study established that the tobacco matrix contains a broad elemental profile and that accumulation cannot be explained by soil concentration alone.

Cadmium provided the clearest example of selective uptake. Reported leaf bioconcentration factors were 7 for Cd, 1.7 for Zn, 1.5 for Cu, 0.12 for Ni and 0.1 for Pb.¹³ The same study reported efficient chloride absorption and translocation under the acidic soil conditions examined and weak correlations between heavy-element mass fractions and measured soil parameters.¹³ Preferential Cd accumulation by *N. tabacum* is also reported in other tobacco-growing systems,²⁶ but quantitative relationships from other regions should not be transferred directly to Mizoram soils.

Principal-component analysis differentiated the northeast Indian tobacco samples from published tobacco profiles from other geographical origins.¹³ This supports the proposition that provenance and cultivation environment can contribute to a characteristic elemental fingerprint. It does not imply that geographical separation by multivariate chemistry is equivalent to a toxicity ranking.

The toxicological relevance of an element in filler depends on its transfer during smoking. Large cigarette datasets show that arsenic, cadmium and lead differ substantially in their distribution among

From product chemistry to biological effect: where direct Zoizal evidence ends

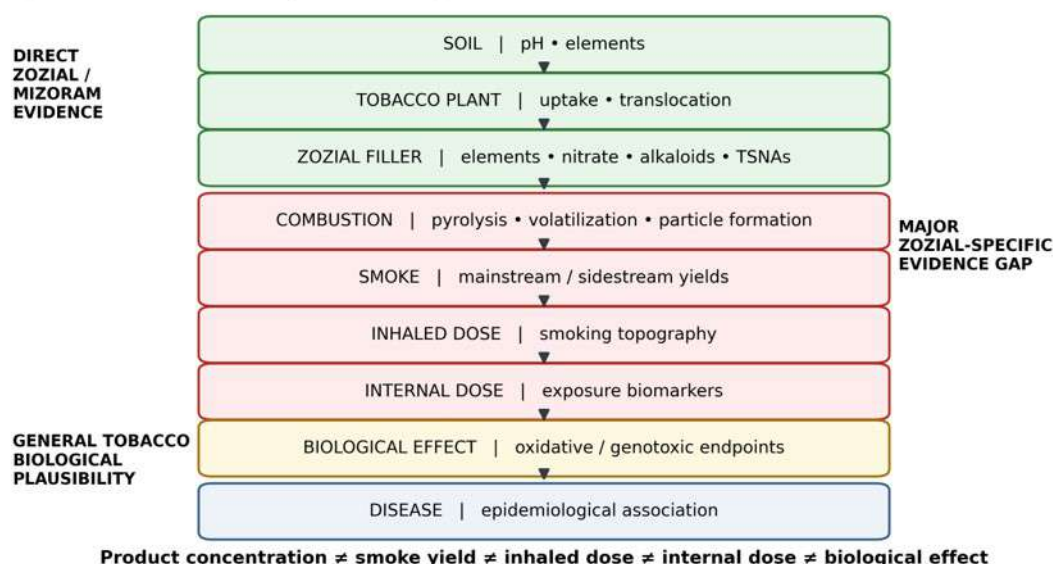


Figure 2. From product chemistry to biological effect: the evidence bridge. Green stages have direct published Zoizal/Mizoram tobacco evidence; red stages identify major Zoizal-specific gaps; amber denotes biological plausibility supported primarily by general tobacco evidence; blue denotes mixed epidemiological evidence. Product concentration should not be treated as equivalent to human dose.

ash, butt, mainstream and sidestream smoke, and that smoking regimen and filter design can materially change measured yields.^{25,27} Those transfer coefficients cannot be assigned to Zozial without direct smoke analysis. Accordingly, the published elemental work establishes a source term—what is present in the tobacco—rather than the inhaled dose. Figure 2 summarizes the evidence bridge from product chemistry to biological effect.

Nitrogen chemistry, alkaloids and tobacco-specific nitrosamines

NNN and NNK are tobacco-specific nitrosamines with established carcinogenic relevance. They can form through nitrosation of tobacco alkaloids during curing, processing and storage, with nitrate/nitrite chemistry and microbial nitrate reduction contributing to nitrosating conditions in tobacco generally.²⁴ Consequently, TSNA concentrations can be influenced by plant nitrogen metabolism and post-harvest processing, although the contribution of each step must be established for the product under study.

Chang et al.²¹ applied three validated isotope-dilution LC-MS/MS methods to 29 smoking tobacco products, including Zozial, bidis, hookah tobaccos and manufactured cigarettes. Within that 29-product dataset, Zozial had the lowest nitrate concentration (705 micrograms/g) and total TSNA concentration (45.2 ng/g). Across the analysed products, nitrate correlated with TSA and TSNA concentrations (reported $r = 0.64\text{--}0.85$, $p < 0.001$), whereas nitrite and pH did not show the same relationship; multiple regression identified nitrate as the primary determinant in the authors' cross-product model.²¹ These are product-composition measurements and should not be interpreted as Zozial smoke yields or as an overall comparative-harm estimate.

This is an important direct Zozial finding, but its interpretation must remain analyte-specific. Low total TSNA relative to the products sampled does not establish low total smoke toxicity. Combustion generates or transfers numerous other toxicants, including carbon monoxide, carbonyls, volatile organic compounds, polycyclic aromatic hydrocarbons, particulate matter and metals.^{1–3} Moreover, the 2026 study measured the tobacco product, not the full Zozial mainstream-smoke toxicant profile. Thus, one important class of tobacco-specific carcinogens has been measured directly in Zozial, but this finding alone cannot be used to compare its overall harmfulness with other smoking products. The two chemical pathways supported by the published evidence are summarized in Figure 3.

Combustion and smoke: the principal unresolved chemical bridge

Unburned tobacco composition and smoke

composition are related but non-equivalent quantities. During heating, pyrolysis and combustion, constituents may volatilize, decompose, react, remain in ash or transfer into particulate and gas phases. Standardized smoking-machine regimens are useful for product comparison but do not reproduce all human smoking behaviour.^{5–8}

Comparative products illustrate why direct Zozial measurements are necessary. Published bidi studies have required product-specific smoking-machine conditions and have quantified nicotine, tar, carbon monoxide and other mainstream-smoke constituents.^{28,29,31} Roll-your-own research likewise shows that hand manufacture does not allow exposure to be predicted from product appearance alone; smoking topography and toxicant uptake require measurement.³⁰ These findings are Class III comparative evidence only. Zozial uses paper rather than tendu leaf and has its own construction and tobacco characteristics, so bidi or roll-your-own emission values must not be substituted for Zozial values.

A future Zozial smoke-characterization study should quantify a defined panel of major smoke constituents under transparent, reproducible smoking regimens. Candidate measurements include nicotine, carbon monoxide, total particulate matter/NFDPM, carbonyls, selected volatile organic compounds, PAHs, TSNA and priority elements. For metals, paired analysis of filler, mainstream smoke, sidestream smoke and ash would permit constituent-specific mass balance. The exact regimen should be justified for Zozial rather than assumed from manufactured cigarettes or bidis.

Smoking topography and delivered dose

Exposure cannot be reconstructed from cigarettes per day alone. Puff count, puff volume, puff duration, interpuff interval, puff velocity, relighting, butt length and inhalation behaviour influence the amount of smoke drawn through a product. Studies of manufactured cigarettes show that smokers can alter puffing intensity in response to product design, and machine-reported low yields can underestimate real-world exposure.^{6–8,32} Total puff volume and related topography measures have been associated with biomarkers such as cotinine, carbon monoxide and NNAL.^{32–34}

This issue is particularly relevant because the thesis described Zozial as having low combustibility and proposed that users may take repeated or deeper puffs to keep it lit.¹⁴ Those statements were not based on a published Zozial smoking-topography study and should therefore be treated as hypotheses rather than established product characteristics. Objective burn-rate measurements and a topography study comparing appropriately defined Zozial and manufactured-cigarette users could directly test puff volume, duration, interval, total puff volume, relighting and butt length.

Two chemical pathways currently supported by published Zozial/Mizoram tobacco evidence

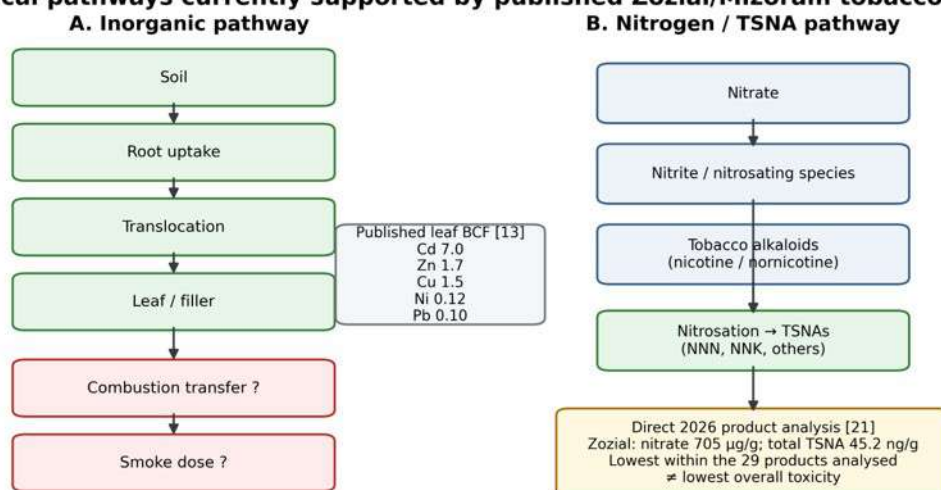


Figure 3. Two chemical pathways supported by the published evidence. (A) Selective elemental accumulation in Mizoram-grown tobacco, with published leaf bioconcentration factors;¹³ combustion transfer and smoke dose remain unmeasured for Zozial. (B) General nitrate-to-TSNA chemistry²⁴ together with the direct 2026 Zozial product measurements.²¹ The comparatively low nitrate and total TSNA values apply only within the 29-product dataset and do not establish lower overall toxicity.

Internal exposure: the missing link between smoke and biological effect

Biomarkers of exposure can bridge product or environmental measurements and internal dose. Nicotine metabolites, including cotinine, are established indicators of nicotine exposure; urinary total NNAL is a tobacco-specific biomarker of NNK uptake, while carbon monoxide measures and metabolites of PAHs or volatile organic compounds can provide complementary information.^{35–37} Such markers quantify exposure or uptake and should not be interpreted as direct measures of disease risk.

For Zozial, an informative biomonitoring strategy would combine a tobacco-specific exposure marker with constituent-class markers rather than relying on a single endpoint. Such measurements should be interpreted as internal dose, not as proof of disease. This distinction becomes especially important when moving from exposure biomarkers to biomarkers of biological effect.

Oxidative stress and oxidative DNA damage: strong plausibility, limited product-specific evidence

Cigarette smoke can impose oxidative burden through radicals already present in smoke, redox-

active smoke constituents, stimulation of cellular ROS-generating systems and disruption of antioxidant defences.³⁸ Oxidative stress can damage lipids, proteins and nucleic acids, providing a mechanistic bridge between exposure and multiple smoking-related pathologies. These mechanisms are well supported for cigarette smoke generally, but they should be classified as Class IV evidence when discussing Zozial.

Urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) is commonly used as a biomarker of oxidative DNA damage. A systematic review and meta-analysis comprising 84 articles and 128 study subgroups found a positive association between smoking and urinary 8-OHdG when concentrations were measured by chemical analytical methods, while also documenting substantial methodological heterogeneity.³⁹ The authors specifically distinguished chemical methods from immunological measurements, an important analytical consideration when comparing studies. This evidence supports 8-OHdG as a biologically relevant tobacco-research endpoint but provides no Zozial-specific effect estimate.

The same restraint applies to antioxidant enzymes such as superoxide dismutase, catalase and glutathione-related systems. Changes in these enzymes may reflect oxidative challenge, adaptation, depletion or differences in biological matrix and assay conditions. A product-specific study therefore requires pre-specified

interpretation, careful confounder control and preferably multiple complementary oxidative-stress endpoints rather than treating a single antioxidant measurement as a direct toxicity scale.

Chromosomal damage and the buccal micronucleus assay

Micronuclei can arise from chromosome fragments or whole chromosomes that are not incorporated into daughter nuclei, and the assay can be applied to exfoliated buccal cells as a minimally invasive biomonitoring method. Because study design, scoring criteria, cell number and confounding can materially affect buccal-micronucleus results, interpretation requires standardized methodology and explicit epidemiological control.^{40,42}

Evidence synthesized across smoking studies indicates higher buccal-cell micronucleus frequencies among smokers than nonsmokers, although substantial methodological variation exists.^{40,41} This supports the assay as a candidate genotoxicity endpoint in tobacco research but does not demonstrate Zoizal-specific chromosomal damage. A Zoizal study would require standardized scoring criteria, adequate cell counts, blinded assessment, clearly defined exposure groups and control of relevant confounders such as age, alcohol use, diet, occupational exposures and other tobacco use.

Epidemiological evidence in Mizoram

Stomach cancer and historical local-cigarette evidence

Phukan et al. conducted a hospital-based case-control study in Mizoram and reported an

adjusted OR of 2.2 (95% CI 1.3–9.3) for participants classified in the original paper as meiziol smokers relative to nonsmokers in the smoking-type analysis.¹⁵ The study also reported higher risk with longer smoking duration and greater cumulative smoking exposure. Because meiziol is a misspelling rather than a separate Mizo product term, the relevance of this study to contemporary Zoizal rests on the physical description of the local cigarette given in the original paper, not on the label itself.

Malakar et al. subsequently conducted a population-based matched case-control study of 102 histologically confirmed stomach-cancer cases and 204 controls. Tobacco smoking was identified as an important risk factor, and the authors used the spelling meiziol for one smoking category and reported it as more important than the other tobacco-related habits examined; GSTM1 and GSTT1 polymorphisms were not directly associated with stomach cancer but were interpreted as possible effect modifiers.¹⁶ Additional Mizoram studies examined interactions of tobacco exposure with p53 codon 72 and CYP2E1 *RsaI* polymorphisms.^{17,18} These studies add local gene-environment evidence but do not establish Zoizal-specific chemical mechanisms, and some reported interaction estimates are imprecise because of small strata.

Lung cancer

The clearest explicitly named Zoizal epidemiological evidence comes from the 2016 Science Vision hospital-based case-control study by Lalpawimawha and Lalruatfela.¹⁹ The study included 106 histologically confirmed lung-cancer cases and 212 matched controls and reported an OR of 2.51 (95% CI 1.28–4.92) for Zoizal smokers. The authors also reported increased risk among participants who had smoked for at least 40 years.

Table 2. Epidemiological evidence relevant to Zoizal. Effect estimates are interpreted only at the exposure specificity supported by each study. Meiziol is retained as printed in the cited studies and is treated here as a misspelling of meizial.

Study	Population/design	Tobacco definition	Outcome	Reported result	What it establishes	What it does not establish
Phukan et al. ¹⁵	Mizoram; stomach cancer case-control	Meiziol (source spelling)	Stomach cancer	Adjusted OR 2.2 (95% CI 1.3–9.3) reported for meiziol smokers; duration/cumulative exposure associations reported	Association with locally described cigarette	Modern Zoizal-specific chemical causation
Malakar et al. ¹⁶	102 cases; 204 matched controls	Local tobacco smoking / meiziol context	Stomach cancer	Tobacco-related associations examined with GSTM1/GSTT1 susceptibility	Smoking-related stomach-cancer evidence in Mizoram	A unique causal effect of Zoizal constituents
Lalpawimawha & Lalruatfela ¹⁹	106 cases; 212 controls	Zoizal	Lung cancer	OR 2.51 (95% CI 1.28–4.92); higher risk reported with long duration of use	Product-specific association in that case-control population	Causality, responsible toxicant, or comparative risk versus cigarettes
Pachau et al. ²⁰	Mizo HNSCC case-control study	Smoking; Zoizal noted among users	Head and neck squamous-cell carcinoma	Smoking OR 6.703 reported; Zoizal use described among patients	Smoking association and local-product context	OR 6.703 as a Zoizal-specific effect

This should be interpreted as an association within that case-control study, not as proof of causality or as a quantified population-wide Zozial risk; exposure classification, residual confounding, selection and recall remain relevant limitations.

Other case-control studies from Mizoram have identified associations involving household wood smoke, cooking-oil fumes, dietary exposures, tobacco smoking and genetic susceptibility.^{43,44} These findings underscore the need for Zozial-specific epidemiology to measure and adjust for locally relevant environmental, dietary and lifestyle co-exposures rather than attributing the regional cancer burden to a single smoking product.

Head and neck cancer

Pachua et al.²⁰ reported significant associations of smoking and alcohol with HNSCC and noted that many patients used locally made alcohol and smoked the local cigarette Zozial. The reported smoking OR of 6.703 was not a Zozial-specific effect estimate. Accordingly, the study provides contextual evidence that Zozial use occurs within the local HNSCC exposure profile, but it cannot quantify the independent risk attributable to Zozial. The epidemiological evidence and the limits of inference from each study are summarized in Table 2.

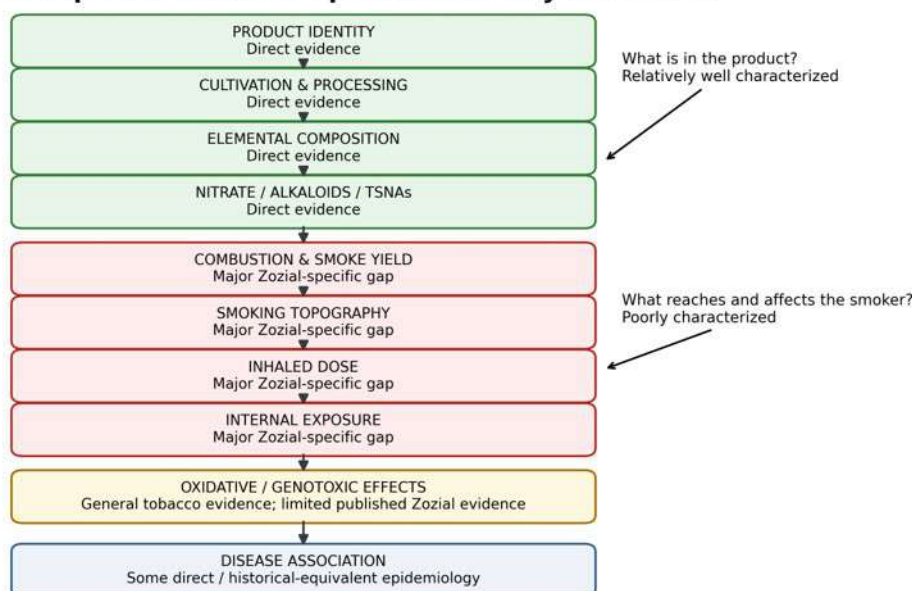
Summary of the available evidence

The available evidence on Zozial is uneven across the exposure pathway. Product identity, traditional processing and the elemental composition of locally grown tobacco have been described directly, and recent analytical work has provided information on nitrate, alkaloids and tobacco-specific nitrosamines. Epidemiological studies from Mizoram also provide some evidence of associations between local smoking practices and cancer, although differences in terminology and exposure definition limit direct comparison between studies. In contrast, important intermediate stages remain poorly studied for Zozial, particularly combustion characteristics, mainstream smoke composition, smoking topography and internal exposure. Evidence concerning oxidative stress and genotoxicity is therefore still derived mainly from studies of other combustible tobacco products. Figure 4 summarizes these areas of direct evidence and the major gaps that remain.

Uncertainty in the comparative harm of Zozial

A valid comparative-harm statement requires integration across multiple dimensions. Product

Evidence map for Zozial: from product identity to disease



Central inference: the evidence chain is incomplete; direct product chemistry should not be converted into unmeasured human dose or mechanism.

Figure 4. Evidence-provenance map for Zozial. Direct evidence is strongest for identity, production and product chemistry, whereas smoke yield, topography and internal exposure remain major product-specific gaps. General tobacco evidence supports biological plausibility, and epidemiological studies provide some direct or historical-equivalent disease-association evidence.^{15–21}

composition alone is inadequate because constituent transfer differs during combustion. Machine smoke yield alone is inadequate because human smoking behaviour varies. Puffing intensity alone is inadequate because products differ in chemistry. Biomarkers of exposure quantify uptake but do not themselves establish disease, while epidemiological outcomes integrate many years of exposure and confounding.

The current evidence therefore contains observations that address different toxicant classes rather than a single overall toxicity scale: within the 29-product dataset analysed in 2026, Zozial had comparatively low nitrate and total TSNA concentrations,²¹ while Mizoram-grown tobacco showed selective Cd accumulation and a distinctive elemental profile.¹³ Neither finding determines overall comparative harm. A lower concentration of one carcinogen class cannot establish safety, and enrichment of another constituent cannot establish greater total harm without evidence on transfer, inhaled dose and biological uptake.

A more defensible conceptual model is: health-relevant exposure = product composition × constituent transfer during smoking × smoking topography × frequency/duration × bioavailability, modified by metabolism, co-exposures and host susceptibility. Several terms in this expression remain unmeasured for Zozial.

Research priorities

Priority 1 – Product standardization. Establish distributions of tobacco mass, dimensions, moisture, paper porosity, pressure drop, burn rate, free-burn time and batch-to-batch chemical variability across producers, seasons and districts.

Priority 2 – Smoke chemistry and mass balance. Quantify mainstream and sidestream emissions under transparent standardized and intensified regimens. Pair filler, smoke and ash analyses for

elements; quantify nicotine, CO, NFDPM/TPM, carbonyls, VOCs, PAHs and TSNA.

Priority 3 – Human smoking topography. Measure puff volume, duration, interval, velocity, puffs per stick, relighting and butt length in naturalistic and laboratory conditions. This would directly test, rather than assume, the thesis-derived hypothesis that Zozial's combustion characteristics may lead to different puffing behaviour.¹⁴

Priority 4 – Biomarkers of exposure. Combine nicotine metabolites with tobacco-specific and toxicant-class markers such as NNAL, CO/COHb, PAH/VOC metabolites and selected metals. Separate biomarkers of exposure from biomarkers of biological effect.

Priority 5 – Biomarkers of biological effect. Oxidative-stress and genotoxicity endpoints should be selected prospectively, analytically validated and interpreted with adequate control for age, sex, diet, alcohol, occupation, environmental smoke and other tobacco use.

Priority 6 – Epidemiology. Future studies should distinguish exclusive Zozial use, exclusive manufactured-cigarette use, dual use, former use and never use; quantify dose and duration; and account for local environmental/dietary co-exposures. Product nomenclature should be explicitly defined in the questionnaire. The principal evidence gaps and the measurements needed to address them are summarized in Table 3.

Implications for scientific communication and tobacco control

Descriptions such as 'traditional', 'local' or 'handmade' should not be interpreted as evidence of reduced harm. Direct analyses show that Zozial tobacco contains measurable TSNA and that Mizoram-grown tobacco has a complex elemental profile that includes toxicologically relevant

Table 3. Research-gap matrix: measurements required to connect Zozial product chemistry with human exposure and health outcomes.

Evidence gap	Why it matters	Required measurement	Suggested approach	Scientific output
Physical standardization	Defines product variability	Mass, dimensions, moisture, paper porosity, pressure drop, burn rate	Multi-batch product characterization	Product specification and variance
Smoke emissions	Converts filler chemistry into emission	Nicotine, CO, particulate matter, VOCs, PAHs, carbonyls, TSNA, metals	Transparent standardized and intensified smoking regimens	Product-specific emission profile
Metal transfer	Leaf concentration ≠ inhaled dose	Matched filler, smoke and ash elemental mass	ICP-MS/OES mass balance	Constituent-specific transfer coefficients
Smoking topography	Determines real-world smoke generation	Puff volume, duration, interval, velocity, count, relighting, butt length	Portable topography in naturalistic/laboratory settings	Realistic use profile
Internal exposure	Confirms systemic uptake	Cotinine plus tobacco-specific/toxicant-class biomarkers	Biomonitoring with exposure control	Internal-dose estimates
Biological effect	Tests mechanistic consequence	Validated oxidative/genotoxic endpoints	Controlled observational studies	Product-specific effect evidence
Disease risk	Links product-specific exposure to outcomes	Detailed exposure history and confounders	Adequately powered epidemiology	Adjusted product-specific risk estimate

constituents.^{13,21} These findings show the presence of chemical hazards, but they do not provide an overall comparison of harm. Conversely, the available evidence also does not justify claiming that Zozial is necessarily more harmful than manufactured cigarettes. For clear scientific communication, findings on product composition should be kept separate from evidence on smoke emissions, internal exposure and disease.

Nomenclature also has practical implications for surveillance. Some historical studies printed meiziol, a misspelling of meizial; the thesis used meizial and Zozial as distinct labels in its operational description; and current scientific work uses Zozial for the indigenous product.^{13–19} Future survey instruments should therefore define the product descriptively and, where feasible, visually rather than relying on a single label. This should reduce exposure misclassification and improve comparability between studies.

Conclusion

Zozial should be considered as a distinct indigenous tobacco product rather than being grouped simply with cigarette smoking. Direct published evidence characterizes its traditional production pathway, the elemental composition of locally cultivated tobacco, selective Cd accumulation, and nitrate, tobacco alkaloid and TSNA concentrations.^{13,21} Epidemiological studies provide an explicitly Zozial-named association with lung cancer and historical local-cigarette evidence relevant to stomach cancer.^{15–19} The major weakness of the evidence base lies between product composition and human biological response: Zozial-specific smoke yields, constituent transfer, smoking topography and internal dose remain insufficiently characterized in the published literature. Studies on cigarette smoking provide biological support for oxidative stress, urinary 8-OHdG and buccal micronuclei as relevant outcomes, but these findings should not be presented as direct evidence for Zozial. Future research should connect the existing product chemistry to measured emissions, actual smoking behaviour, internal exposure and rigorously designed biological and epidemiological studies. Until these links are measured directly, there is not enough evidence to conclude that Zozial is either safer or more harmful overall than manufactured cigarettes.

Conflict of interests

The authors declare no competing interests.

References

1. International Agency for Research on Cancer. (2012). Personal habits and indoor combustions.

- IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, 100E. Lyon, France: IARC.
2. World Health Organization. (2019). The Tobacco Body. Geneva, Switzerland: World Health Organization.
3. Centers for Disease Control and Prevention. (2024). Health effects of cigarettes: Cancer. <https://www.cdc.gov/tobacco/about/cigarettes-and-cancer.html> (29 September 2026).
4. Adam, T., McAughey, J., Mocker, C., McGrath, C., Zimmermann, R. (2010). Influence of filter ventilation on the chemical composition of cigarette mainstream smoke. *Analytica Chimica Acta*, **657**, 36–44. <https://doi.org/10.1016/j.aca.2009.10.015>
5. Kozlowski, L.T., O'Connor, R.J. (2002). Cigarette filter ventilation is a defective design because of misleading taste, bigger puffs, and blocked vents. *Tobacco Control*, **11**(Supp 1), i40–i50. https://doi.org/10.1136/tc.11.suppl_1.i40
6. Song, M.A., Benowitz, N.L., Berman, M., et al. (2017). Cigarette filter ventilation and its relationship to increasing rates of lung adenocarcinoma. *Journal of the National Cancer Institute*, **109**, dx075.
7. Appleton, S., Liu, J., Lipowicz, P.J., Sarkar, M. (2015). Effect of cigarette design on biomarkers of exposure, puffing topography and respiratory parameters. *Inhalation Toxicology*, **27**, 174–180. <https://doi.org/10.3109/08958378.2015.1021980>
8. Bridges, R.B., Combs, J.G., Humble, J.W., Turbek, J.A., Rehm, S.R., Haley, N.J. (1990). Puffing topography as a determinant of smoke exposure. *Pharmacology Biochemistry and Behavior*, **37**, 29–39. [https://doi.org/10.1016/0091-3057\(90\)90037-I](https://doi.org/10.1016/0091-3057(90)90037-I)
9. Chaturvedi, H.K., Phukan, R.K., Zoramtharga, K., Hazarika, N.C., Mahanta, J. (1998). Tobacco use in Mizoram, India: sociodemographic differences in pattern. *Southeast Asian Journal of Tropical Medicine and Public Health*, **29**, 66–70.
10. Zomawia, E., Zuala, S., Hmangaihuali, E.V.L., Pachauu, L. (2025). Monitoring survey of cancer risk factors and health system response in Northeast Region, Mizoram. *Indian Journal of Public Health*, **69**, 405–410. https://doi.org/10.4103/ijph.ijph_244_24
11. Nath, A., SathishKumar, K., Das, P., et al. (2023). Need for accelerating tobacco control in India: findings from the National Cancer Registry Programme. *European Journal of Cancer Prevention*, **32**, 184–194. <https://doi.org/10.1097/CEJ.0000000000000759>
12. Harris, C., Das, G., Mukherjee, P. (2022). Development of cancer care in Northeast India.

- Indian Journal of Surgical Oncology*, **13(Suppl 1)**, 61–66. <https://doi.org/10.1007/s13193-022-01557-z>
13. Lalrammawia, K., Buragohain, A., Kakki, B., Zote, L., Marak, N.K., Lalrinhlupuii, et al. (2022). Determination of multi elements in tobacco plant of Northeast India by neutron activation analysis and atomic absorption spectrometry. *Biological Trace Element Research*, **200**, 4534–4549. <https://doi.org/10.1007/s12011-021-03040-2>
 14. Lalrammawia, K. (2021). Physico-chemical characterization and the evaluation of oxidative potential of Zozial, the indigenous hand-rolled cigarette of Mizoram. PhD thesis. Aizawl, India: Mizoram University.
 15. Phukan, R.K., Zomawia, E., Narain, K., Hazarika, N.C., Mahanta, J. (2005). Tobacco use and stomach cancer in Mizoram, India. *Cancer Epidemiology, Biomarkers & Prevention*, **14**, 1892–1896. <https://doi.org/10.1158/1055-9965.EPI-05-0074>
 16. Malakar, M., Devi, K.R., Phukan, R.K., et al. (2012). Genetic polymorphism of glutathione S-transferases M1 and T1, tobacco habits and risk of stomach cancer in Mizoram, India. *Asian Pacific Journal of Cancer Prevention*, **13**, 4725–4732. <https://doi.org/10.7314/APJCP.2012.13.9.4725>
 17. Malakar, M., Devi, K.R., Phukan, R.K., et al. (2014). p53 codon 72 polymorphism interactions with dietary and tobacco related habits and risk of stomach cancer in Mizoram, India. *Asian Pacific Journal of Cancer Prevention*, **15**, 717–723. <https://doi.org/10.7314/APJCP.2014.15.2.717>
 18. Malakar, M., Devi, K.R., Phukan, R.K., et al. (2014). CYP2E1 genetic polymorphism with dietary, tobacco, alcohol habits, H. pylori infection status and susceptibility to stomach cancer in Mizoram, India. *Asian Pacific Journal of Cancer Prevention*, **15**, 8815–8822. <https://doi.org/10.7314/APJCP.2014.15.20.8815>
 19. Lalpawimawha, Lalruatfela, B. (2016). Etiology of lung cancer among the Mizo people. *Science Vision*, **16**, 113–122.
 20. Pachua, L., Zami, Z., Nunga, T., et al. (2022). First-degree family history of cancer can be a potential risk factor among head and neck cancer patients in an isolated Mizo tribal population, northeast India. *Clinical Epidemiology and Global Health*, **13**, 100954. <https://doi.org/10.1016/j.cegh.2021.100954>
 21. Chang, Y.J., Muthukumaran, R.B., Lalrinhlupuii, Wang, Y.J., Zote, L., Kakki, B., Hu, C.W., Chao, M.R. (2026). Nitrate as an indicator of tobacco-specific alkaloid and nitrosamine content in smoking tobacco products. *Industrial Crops and Products*, **250**, 123914. <https://doi.org/10.1016/j.indcrop.2026.123914>
 22. Lalruatfela, B. (2019). A review on tobacco and its effect on health. *Science Vision*, **19**, 16–23. <https://doi.org/10.33493/scivis.19.01.04>
 23. Nath, A., Mathur, P. (2022). Strengthening cancer surveillance in India: role of the National Cancer Registry Programme. *Indian Journal of Surgical Oncology*, **13(Suppl 1)**, 2–7. <https://doi.org/10.1007/s13193-021-01473-8>
 24. Peterson, L.A., Stanfill, S.B., Hecht, S.S. (2024). An update on the formation in tobacco, toxicity and carcinogenicity of N'-nitrosonornicotine and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone. *Carcinogenesis*, **45**, 275–287. <https://doi.org/10.1093/carcin/bgae018>
 25. Piadé, J.J., Jaccard, G., Dolka, C., Belushkin, M., Wajrock, S. (2015). Differences in cadmium transfer from tobacco to cigarette smoke, compared to arsenic or lead. *Toxicology Reports*, **2**, 12–26. <https://doi.org/10.1016/j.toxrep.2014.11.005>
 26. Lu, X., Zhang, D., Ugurlu, A., Chen, Y., Proshad, R. (2021). Bioaccumulation of cadmium in *Nicotiana tabacum* L. (tobacco) characterized by soil properties: a case study in the Sichuan Basin, China. *Analytical Letters*, **54**, 2883–2894. <https://doi.org/10.1080/00032719.2021.1900215>
 27. Pappas, R.S., Polzin, G.M., Zhang, L., Watson, C.H., Paschal, D.C., Ashley, D.L. (2006). Cadmium, lead, and thallium in mainstream tobacco smoke particulate. *Food and Chemical Toxicology*, **44**, 714–723. <https://doi.org/10.1016/j.fct.2005.10.004>
 28. Watson, C.H., Polzin, G.M., Calafat, A.M., Ashley, D.L. (2003). Determination of tar, nicotine, and carbon monoxide yields in the smoke of bidi cigarettes. *Nicotine & Tobacco Research*, **5**, 747–753. <https://doi.org/10.1080/1462220031000158591>
 29. Oladipupo, O.A., Dutta, D., Chong, N.S. (2019). Analysis of chemical constituents in mainstream bidi smoke. *BMC Chemistry*, **13**, 93. <https://doi.org/10.1186/s13065-019-0614-7>
 30. Koszowski, B., Rosenberry, Z.R., Viray, L.C., Potts, J.L., Pickworth, W.B. (2014). Make your own cigarettes: toxicant exposure, smoking topography, and subjective effects. *Cancer Epidemiology, Biomarkers & Prevention*, **23**, 1793–1803. <https://doi.org/10.1158/1055-9965.EPI-14-0280>
 31. Sharma, P., Kaur, J., Rinkoo, A.V., Rao, V., Salam, A., Fayokun, R., Murthy, P. (2026). Analysis of nicotine, tar, carbon monoxide, total particulate matter, water, benzo[a]pyrene, and humectants in cigarettes and bidis from India and Myanmar.

- Scientific Reports*, **16**, 6775. <https://doi.org/10.1038/s41598-026-35417-5>
32. Matsumoto, M., Inaba, Y., Yamaguchi, I., Endo, O., Hammond, D., Uchiyama, S., Suzuki, G. (2013). Smoking topography and biomarkers of exposure among Japanese smokers: associations with cigarette emissions obtained using machine smoking protocols. *Environmental Health and Preventive Medicine*, **18**, 95–103. <https://doi.org/10.1007/s12199-012-0293-7>
 33. Kim, S., Yu, S. (2018). Smoking topography among Korean smokers: intensive smoking behavior with larger puff volume and shorter interpuff interval. *International Journal of Environmental Research and Public Health*, **15**, 1024. <https://doi.org/10.3390/ijerph15051024>
 34. Strasser, A.A., Benowitz, N.L., Pinto, A.G., et al. (2011). Nicotine metabolite ratio predicts smoking topography and carcinogen biomarker level. *Cancer Epidemiology, Biomarkers & Prevention*, **20**, 234–238. <https://doi.org/10.1158/1055-9965.EPI-10-0674>
 35. Benowitz, N.L. (1999). Biomarkers of environmental tobacco smoke exposure. *Environmental Health Perspectives*, **107** (Suppl 2), 349–355. <https://doi.org/10.1289/ehp.99107s2349>
 36. Avila-Tang, E., Al-Delaimy, W.K., Ashley, D.L., et al. (2013). Assessing secondhand smoke using biological markers. *Tobacco Control*, **22**, 164–171. <https://doi.org/10.1136/tobaccocontrol-2011-050298>
 37. Marques, H., Cruz-Vicente, P., Rosado, T., Barroso, M., Passarinha, L.A., Gallardo, E. (2021). Recent developments in the determination of biomarkers of tobacco smoke exposure in biological specimens: a review. *International Journal of Environmental Research and Public Health*, **18**, 1768. <https://doi.org/10.3390/ijerph18041768>
 38. Seo, Y.S., Park, J.M., Kim, J.H., Lee, M.Y. (2023). Cigarette smoke-induced reactive oxygen species formation: a concise review. *Antioxidants*, **12**, 1732. <https://doi.org/10.3390/antiox12091732>
 39. Graille, M., Wild, P., Sauvain, J.J., Hemmendinger, M., Guseva Canu, I., Hopf, N.B. (2020). Urinary 8-OHdG as a biomarker for oxidative stress: a systematic literature review and meta-analysis. *International Journal of Molecular Sciences*, **21**, 3743. <https://doi.org/10.3390/ijms21113743>
 40. de Geus, J.L., Wambier, L.M., Bortoluzzi, M.C., Loguercio, A.D., Kossatz, S., Reis, A. (2018). Does smoking habit increase the micronuclei frequency in the oral mucosa of adults compared to non-smokers? A systematic review and meta-analysis. *Clinical Oral Investigations*, **22**, 81–91. <https://doi.org/10.1007/s00784-017-2246-4>
 41. Abdul, N.S., Alrukban, N.K., Alajmi, A.M., Bindawoad, F.A., Almughaiseeb, A.A., AlGhannam, S.M. (2022). Cytotoxic and genotoxic effects of cigarette and waterpipe tobacco smoking on buccal mucosa: a systematic review and meta-analysis. *Journal of Oral and Maxillofacial Pathology*, **26**, 534–540. https://doi.org/10.4103/jomfp.jomfp_292_22
 42. Knasmüller, S., Nersesyan, A., Mišík, M., et al. (2026). The micronucleus assay in exfoliated buccal cells induced by lifestyle factors: an overview. *Mutagenesis*, **41**, 46–72. <https://doi.org/10.1093/mutage/geag008>
 43. Phukan, R.K., Saikia, B.J., Borah, P.K., Zomawia, E., Sekhon, G.S., Mahanta, J. (2014). Role of household exposure, dietary habits and glutathione S-transferases M1, T1 polymorphisms in susceptibility to lung cancer among women in Mizoram India. *Asian Pacific Journal of Cancer Prevention*, **15**, 3253–3260. <https://doi.org/10.7314/APJCP.2014.15.7.3253>
 44. Saikia, B.J., Das, M., Sharma, S.K., et al. (2014). Association of a p53 codon 72 gene polymorphism with environmental factors and risk of lung cancer: a case control study in Mizoram and Manipur, a high incidence region in North East India. *Asian Pacific Journal of Cancer Prevention*, **15**, 10653–10658. <https://doi.org/10.7314/APJCP.2014.15.24.10653>