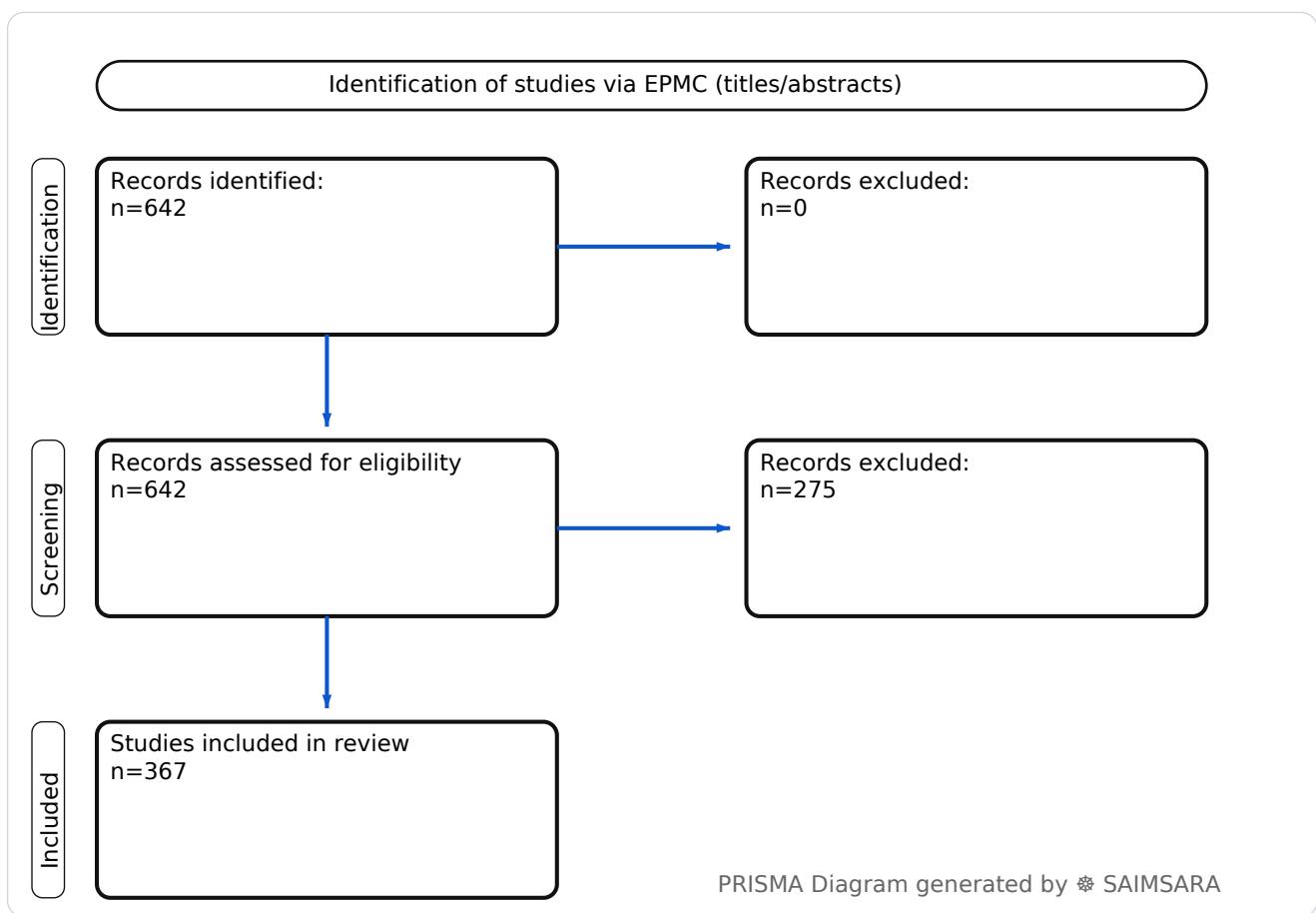


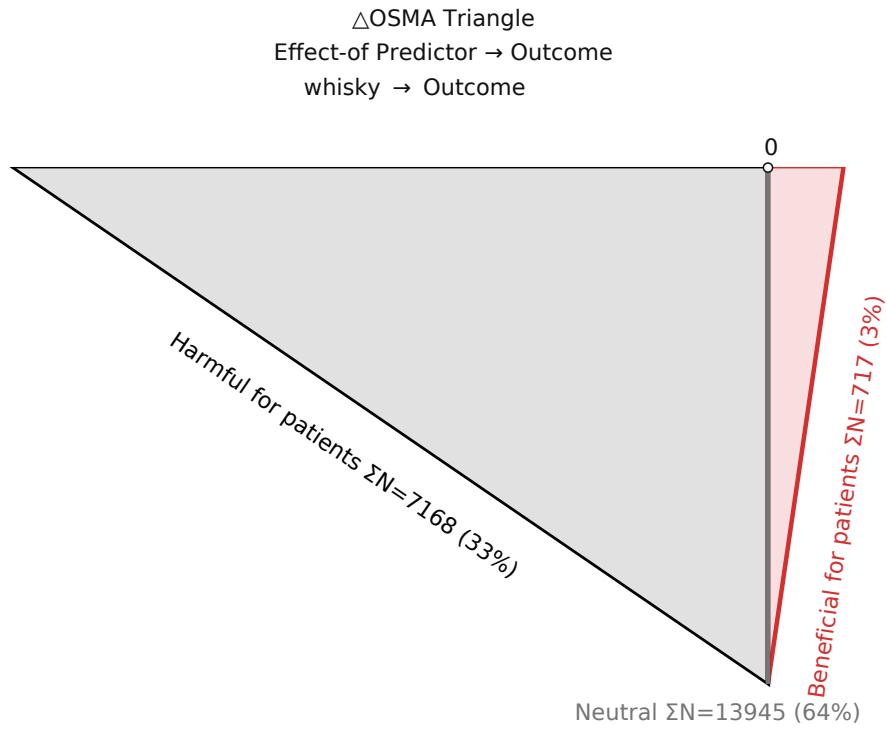
Whisky: Systematic Review with SAIMSARA.

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Review Stats

- Generated: 2025-12-25 14:46:14 CET
- Plan: Premium (expanded craft tokens; source: Europe PMC)
- Source: Europe PMC
- Scope: Titles/Abstracts (tiab)
- Keyword Gate: Fuzzy ($\geq 60\%$ of required terms, minimum 2 terms matched in title/abstract)
- Total Abstracts/Papers: 642
- Downloaded Abstracts/Papers: 642
- Included original Abstracts/Papers: 367
- Total study participants (naïve ΣN): 21830





△OSMA Triangle generated by ♠SAIMSARA

Outcome-Sentiment Meta-Analysis (OSMA): (LLM-only)

Frame: Effect-of Predictor → Outcome • *Source:* Europe PMC

Outcome: Outcome Typical timepoints: 45-y, 60-day. Reported metrics: %, CI, p.

Common endpoints: Common endpoints: mortality, complications, functional.

Predictor: whisky — exposure/predictor. Doses/units seen: 67 mg, 0 mg, 35 ml, 5.46 kg, 500 ml, 30 ml.... Routes seen: topical, oral, intravenous, inhaled. Typical comparator: original ones, control, no treatment, fasted state conditions....

- **1) Beneficial for patients** — Outcome with whisky — [88], [146], [152], [237], [288], [292] — $\Sigma N=717$
- **2) Harmful for patients** — Outcome with whisky — [7], [42], [55], [63], [78], [92], [93], [95], [98], [105], [123], [134], [153], [160], [167], [193], [222], [223], [233], [274], [277], [283], [285], [286], [304], [306], [311], [315], [323], [338], [339], [351], [356], [362], [364] — $\Sigma N=7168$
- **3) No clear effect** — Outcome with whisky — [1], [2], [3], [4], [5], [6], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23], [24], [25], [26], [27], [28], [29], [30], [31], [32], [33], [34], [35], [36], [37], [38], [39], [40], [41], [43], [44], [45], [46], [47], [48], [49], [50], [51], [52], [53], [54], [56], [57], [58], [59], [60],

[61], [62], [64], [65], [66], [67], [68], [69], [70], [71], [72], [73], [74], [75], [76], [77], [79], [80], [81], [82], [83], [84], [85], [86], [87], [89], [90], [91], [94], [96], [97], [99], [100], [101], [102], [103], [104], [106], [107], [108], [109], [110], [111], [112], [113], [114], [115], [116], [117], [118], [119], [120], [121], [122], [124], [125], [126], [127], [128], [129], [130], [131], [132], [133], [135], [136], [137], [138], [139], [140], [141], [142], [143], [144], [145], [147], [148], [149], [150], [151], [154], [155], [156], [157], [158], [159], [161], [162], [163], [164], [165], [166], [168], [169], [170], [171], [172], [173], [174], [175], [176], [177], [178], [179], [180], [181], [182], [183], [184], [185], [186], [187], [188], [189], [190], [191], [192], [194], [195], [196], [197], [198], [199], [200], [201], [202], [203], [204], [205], [206], [207], [208], [209], [210], [211], [212], [213], [214], [215], [216], [217], [218], [219], [220], [221], [224], [225], [226], [227], [228], [229], [230], [231], [232], [234], [235], [236], [238], [239], [240], [241], [242], [243], [244], [245], [246], [247], [248], [249], [250], [251], [252], [253], [254], [255], [256], [257], [258], [259], [260], [261], [262], [263], [264], [265], [266], [267], [268], [269], [270], [271], [272], [273], [275], [276], [278], [279], [280], [281], [282], [284], [287], [289], [290], [291], [293], [294], [295], [296], [297], [298], [299], [300], [301], [302], [303], [305], [307], [308], [309], [310], [312], [313], [314], [316], [317], [318], [319], [320], [321], [322], [324], [325], [326], [327], [328], [329], [330], [331], [332], [333], [334], [335], [336], [337], [340], [341], [342], [343], [344], [345], [346], [347], [348], [349], [350], [352], [353], [354], [355], [357], [358], [359], [360], [361], [363], [365], [366], [367] — $\Sigma N=13945$

1) Introduction

Whisky, a globally significant distilled alcoholic beverage, is a subject of extensive scientific inquiry spanning its complex chemical composition, production processes, sensory attributes, authentication, and diverse impacts on human health and the environment. Recent research highlights the evolving landscape of whisky, from the emergence of new regional varieties like Chinese whisky [1] to advanced analytical techniques for quality control and counterfeit detection [4, 102]. Understanding the intricate interplay of raw materials, fermentation, maturation, and consumption patterns is crucial for both the industry and public health. This paper synthesizes current research to delineate key themes and identify critical gaps in the scientific understanding of whisky.

2) Aim

To systematically review and synthesize recent academic literature concerning whisky, extracting key findings related to its composition, production, analysis, health implications, and environmental

aspects, and to identify emergent research topics and future directions.

3) Methods

Systematic review with multilayer AI research agent: keyword normalization, retrieval & structuring, and paper synthesis (see SAIMSARA About section for details).

- **Bias:** Qualitatively inferred from study design fields. A notable proportion of studies employed mixed designs or did not specify directionality, often lacking detailed population or sample size information, which may limit generalizability and inferential strength, particularly in human health and environmental contexts.

4) Results

4.1 Study characteristics:

The studies predominantly utilized mixed designs, often integrating chemical analysis with other methodologies, and frequently lacked specified directionality. Cohort and cross-sectional studies were also observed, particularly in human health and environmental contexts. Populations varied widely, encompassing yeast strains during fermentation [3, 5], commercial whisky samples [4, 11], human adults [7, 10, 16], rats and mice [10, 63, 105], and specific barley cultivars [19, 20]. Follow-up periods were largely not specified, or varied from short durations (e.g., 2 hours for alcohol metabolism [76]) to long-term observations (e.g., 36 months for spirit aging [23], up to 43 years for maturation impact [56]).

4.2 Main numerical result aligned to the query:

Machine learning models and various spectroscopic and mass spectrometric techniques demonstrated high accuracy in whisky identification, classification, and authentication. The median accuracy reported across these diverse methods was 97.86% [8, 15], with a range spanning 92% [41] to 100% [54] for distinguishing between brands, origins, or authentic versus counterfeit samples. For instance, portable Raman spectroscopy achieved over 99% accuracy in brand identification [4], while sensory evaluation and analytical procedures distinguished Scotch from American whiskies with 97.86% and 96.94% accuracy, respectively [8, 15]. A bimetallic nanoplasmonic tongue differentiated whiskies with over 99.7% accuracy [102], and SWIR hyperspectral imaging achieved 99.8% accuracy for phenolic compound levels in peated barley malt [113].

4.3 Topic synthesis:

- **Flavor and Aroma Chemistry:** Whisky lactones (cis- and trans-) are key aroma compounds, contributing coconut-like, woody, and fruity notes [2, 24, 32, 37, 100, 118, 120, 124, 132, 136, 139, 141, 143, 165, 176, 200, 206, 207, 210, 234, 263, 264]. Their

enantiomeric purity and ratio are influenced by oak aging and microbial processes [69, 81, 117, 118, 124, 198, 199]. Other significant aroma markers include pyrazines, lactones, and furans [17], sulfur compounds [52, 108], and bromophenols in peated whiskies [40, 129]. Dilution impacts the balance of hydrophilic and hydrophobic aroma compounds [11].

- **Authentication and Adulteration Detection:** Advanced analytical techniques, including machine learning with portable Raman spectroscopy [4], rapid sensory and chemical analysis [8, 15], elemental profiling [18, 44, 59], ¹H NMR spectroscopy [33, 45], mass spectrometry (FT-ICR-MS, DAPCI-MS, GC-HRMS, ESI-MS) [38, 41, 56, 62, 65, 66, 73, 110, 151], and near-infrared instruments [12, 154], achieve high accuracy (e.g., >99% [4, 102]) in identifying whisky brands, origins, age, and detecting adulterants like methanol [12, 34, 47, 260], paracetamol [9], and other contaminants [74, 94]. Stable isotope analysis also discriminates authentic from counterfeit Scotch whisky [99, 127].
- **Production and Fermentation Processes:** Yeast strains, particularly *Saccharomyces cerevisiae*, are critical for fermentation, with specific strains used in American whisky production engineered for enhanced heme production [5]. Nitrogen sources, including peptides, are utilized by yeast during Scotch grain whisky fermentation [3]. Barley quality, influenced by factors like algal fertilizer [19] and novel genetic lines [20], is crucial for malt and spirit yield [135, 142, 163, 212]. Wort pretreatments impact flavor development [25]. Lactic acid bacteria, such as *Lactiplantibacillus plantarum* [27, 89, 214, 215, 225], play a role in mash fermentation and flavor profile, including the conversion of unsaturated fatty acids to lactone precursors [219, 220]. Maturation in oak barrels, including Sherry Casks® and Mongolian oak, significantly influences chemical and sensory profiles, contributing unique volatile and phenolic compounds [1, 23, 30, 38, 53, 56, 115, 118, 120, 136, 165, 176, 200, 206, 210, 234, 238, 239, 267].
- **Health and Societal Impacts:** Whisky consumption has been linked to various health outcomes, including a J-shaped curve association with colorectal cancer risk [22] and bone strength [276], and increased risk of esophageal cancer [311, 323, 339]. Regular consumption of adulterated whisky is a significant risk factor for alcoholism [7]. Moderate consumption may increase plasma adiponectin levels and improve insulin sensitivity [288, 292], and whisky congeners have shown anti-melanogenic [103, 126], anti-oxidative [91, 106, 107], anti-inflammatory, and anti-diabetes potential [58, 152]. However, it can cause gastric mucosal injury [167, 222, 251, 360], affect gastric emptying [16, 36, 71, 80, 116, 178], and impact the gut microbiome [10]. Alcohol advertising, including for whisky, targets younger and heavy drinkers [87, 125].
- **Environmental and Resource Management:** Whisky distilleries generate significant co-products and waste streams, such as pot ale, spent wash, and draff [13, 26, 180, 184, 185, 216, 231, 330, 331]. These can be valorized for biomethane production [31, 84, 226], hydrogen production [13], protein, lactic acid, and mineral recovery [26], or as substrates

for fungal biopesticides [90]. Constructed wetlands [6, 224] and heat recovery systems [43] are effective for wastewater treatment and reducing carbon emissions and water scarcity impacts.

- **Sensory Perception and Consumer Behavior:** Whisky lactones can modulate perceived astringency [2] and influence red wine fruity aroma [32]. Dilution affects aroma perception [11, 57]. Sensory evaluation methods can distinguish whiskies by origin and type [8, 15, 70, 253, 254, 296]. Consumer preferences are influenced by factors like glassware congruency [145] and the introduction of lower-strength variants [39].

- **Analytical Methodologies:** A wide array of analytical techniques are employed, including various mass spectrometry approaches (FT-ICR-MS, GC-HRMS, SIFT-MS, DAPCI-MS, ESI-MS) [38, 41, 56, 62, 65, 66, 73, 75, 108, 110, 112, 127, 129, 151, 155, 170, 190, 198, 230, 232], spectroscopic methods (Raman, NIR, FT-IR, UV-Vis, ICP-MS, TXRF) [4, 12, 18, 44, 46, 47, 54, 59, 67, 70, 96, 97, 113, 119, 154, 157, 171, 174], NMR spectroscopy [33, 45, 186, 218], and electronic nose systems [83, 196, 228]. These methods facilitate compound quantification, origin discrimination, and adulteration detection.

5) Discussion

5.1 Principal finding:

Diverse analytical techniques, including machine learning models, spectroscopy, and mass spectrometry, consistently achieve high accuracy in whisky identification, classification, and authentication, with a median accuracy of 97.86% [8, 15] and a range of 92% [41] to 100% [54].

5.2 Clinical implications:

- **Adulterated Whisky Risk:** Regular consumption of adulterated whisky is a significant risk factor for alcoholism and other health issues, necessitating robust detection methods and public health warnings [7, 9, 12, 18, 34, 47, 55, 59, 74, 78, 94, 98, 99, 110, 151, 162, 218, 260, 273].
- **Alcohol-Related Health Outcomes:** Whisky consumption is associated with varying health effects, including potential J-shaped curves for colorectal cancer and bone strength [22, 276], increased risk of esophageal cancer [311, 323, 339], and gastric mucosal injury [167, 222, 251, 360]. Clinicians should counsel patients on these risks, especially for high-alcohol beverages.
- **Gastric Physiology and Drug Interactions:** Whisky can influence gastric emptying [16, 36, 71, 80, 116, 178] and may interact with drug metabolism (e.g., paracetamol toxicity [274], doxycycline absorption [340]) or induce specific physiological responses (e.g., calcitonin secretion [284, 293, 333]).

- **Dental Health and Material Degradation:** Whisky can cause significant degradation in the surface hardness, roughness, and erosion of dental resin composites [92, 111, 153, 160, 235, 281], suggesting implications for dental care and material selection.
- **Emergency Medicine:** Whisky has been used as an oral ethanol treatment for ethylene glycol intoxication when standard medical treatments are unavailable [82, 159], highlighting its potential role in specific emergency scenarios.

5.3 Research implications / key gaps:

- **Longitudinal Health Studies:** Further prospective cohort studies are needed to clarify the long-term health impacts of specific whisky consumption patterns (e.g., moderate vs. heavy, pure vs. adulterated) across diverse populations and age groups [22, 276, 311, 323, 339].
- **Mechanism of Congener Effects:** Research should further elucidate the precise mechanisms by which whisky congeners exert their observed biological effects, such as anti-melanogenic, anti-oxidative, and gastric protective activities, and their interactions with human physiology [58, 88, 103, 106, 126, 140, 146, 152, 194, 258, 288, 292].
- **Standardized Adulteration Benchmarks:** Development of standardized reference materials and universally accepted detection thresholds for common adulterants (e.g., methanol, paracetamol) is crucial to enhance the reliability and comparability of authentication methods across different regions and regulatory bodies [9, 12, 34, 47, 260].
- **Microbiome-Metabolome Interactions:** Deeper investigation into the specific non-ethanolic components of whisky and their differential impact on the gut microbiome and metabolome is warranted to understand observed changes in gut health markers [10].
- **Sustainable Production Optimization:** Research is needed to optimize resource recovery and waste treatment technologies for whisky distillery co-products, focusing on scalability, economic viability, and broader environmental benefits beyond pilot studies [13, 26, 31, 43, 84, 90, 184, 185, 226, 231].

5.4 Limitations:

- **Study Design Heterogeneity** — The review included diverse study designs, many of which were mixed or did not specify directionality, limiting the ability to draw strong causal inferences.
- **Population Specificity** — Many human studies were conducted on specific populations (e.g., healthy male volunteers, specific patient groups), which may limit the generalizability of findings to broader demographics.

- **Sample Size Variability** — A significant number of studies did not report sample sizes or used small sample sizes, particularly in experimental settings, which can affect the statistical power and robustness of results.
- **Qualitative Bias Inference** — Bias was qualitatively inferred due to the absence of explicit bias assessment in the structured summary, potentially overlooking specific methodological weaknesses.
- **Incompatible Numeric Outcomes** — Direct quantitative meta-analysis was not feasible for many outcomes due to heterogeneity in metrics, units, and comparators, necessitating qualitative synthesis for several topics.

5.5 Future directions:

- **Clinical Population Studies** — Conduct large-scale, diverse population studies.
- **Standardized Adulteration Benchmarks** — Develop universal detection thresholds for adulterants.
- **Microbiome Impact Mechanisms** — Investigate specific whisky components affecting gut health.
- **Sustainable Production Scalability** — Evaluate large-scale implementation of waste valorization.
- **Flavor Compound Synthesis** — Explore novel, environmentally friendly lactone production.

6) Conclusion

Diverse analytical techniques, including machine learning models, spectroscopy, and mass spectrometry, consistently achieve high accuracy in whisky identification, classification, and authentication, with a median accuracy of 97.86% [8, 15] and a range of 92% [41] to 100% [54]. These findings are generally applicable to commercial whisky products and various geographical origins, supporting quality control and consumer protection. However, the heterogeneity in study designs and populations represents the most significant limitation affecting the certainty and generalizability of some findings. Therefore, future research should prioritize the development of standardized adulteration benchmarks to ensure public safety and product integrity globally.

References

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Figure 1. Publication-year distribution of included originals

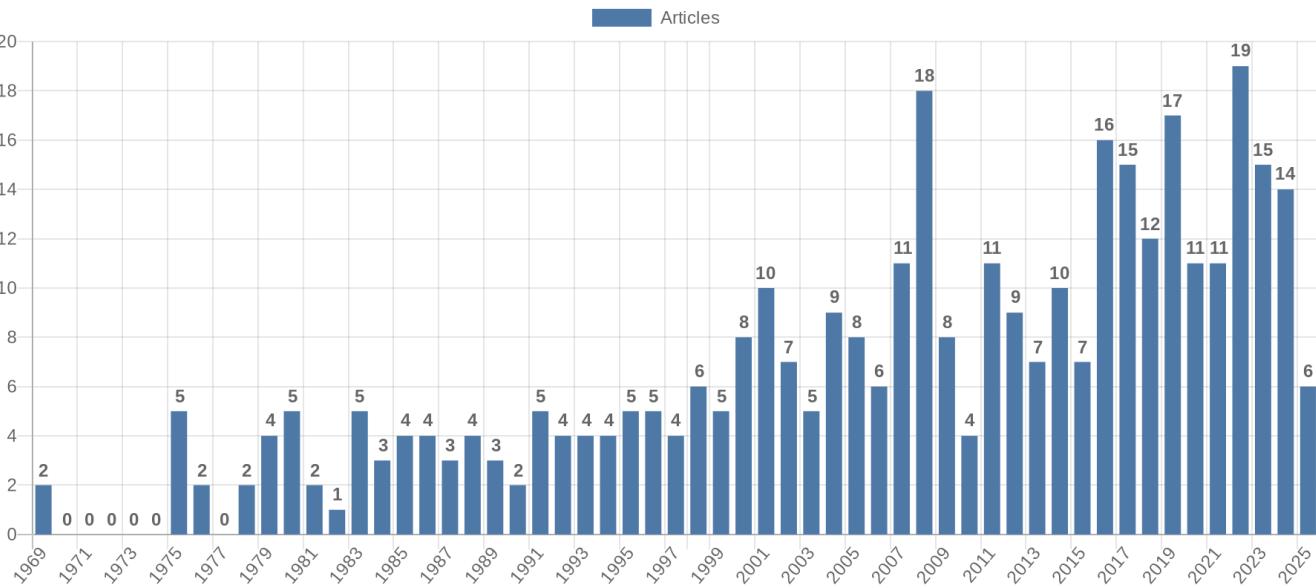


Figure 2. Study-design distribution of included originals

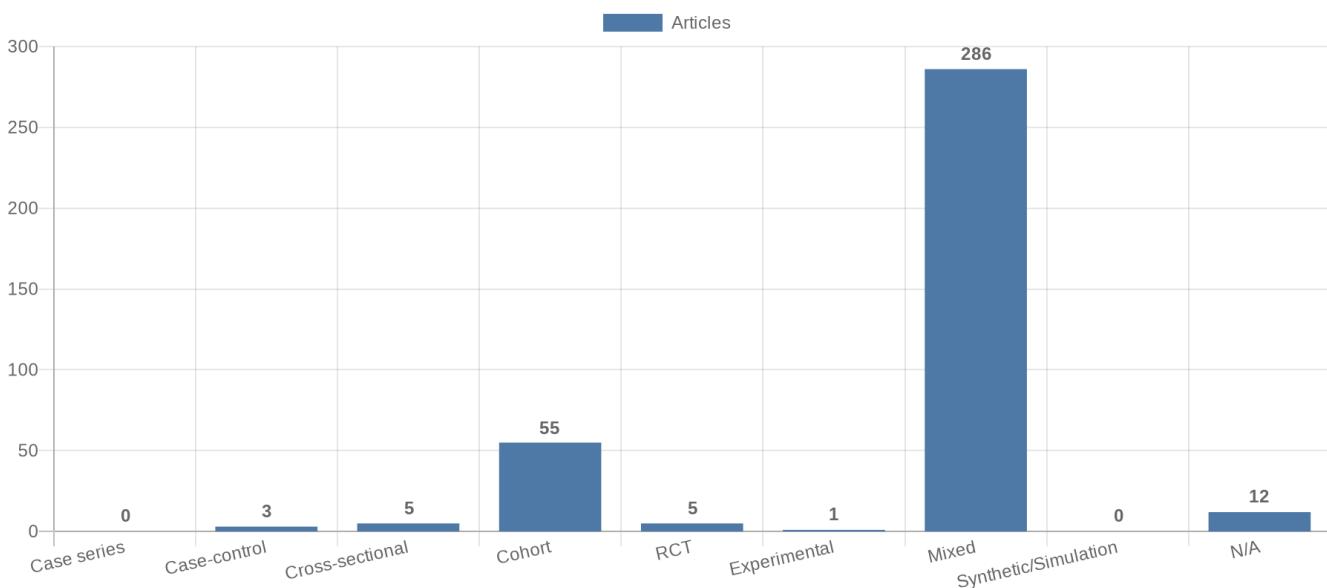


Figure 3. Study-type (directionality) distribution of included originals

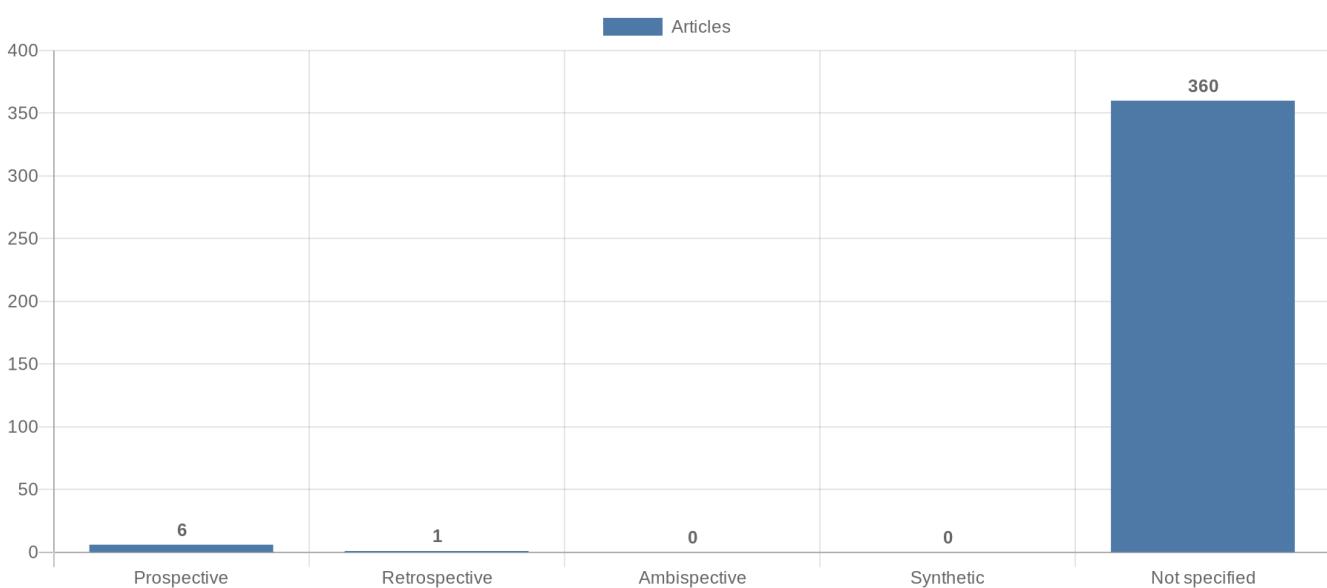


Figure 4. Main extracted research topics

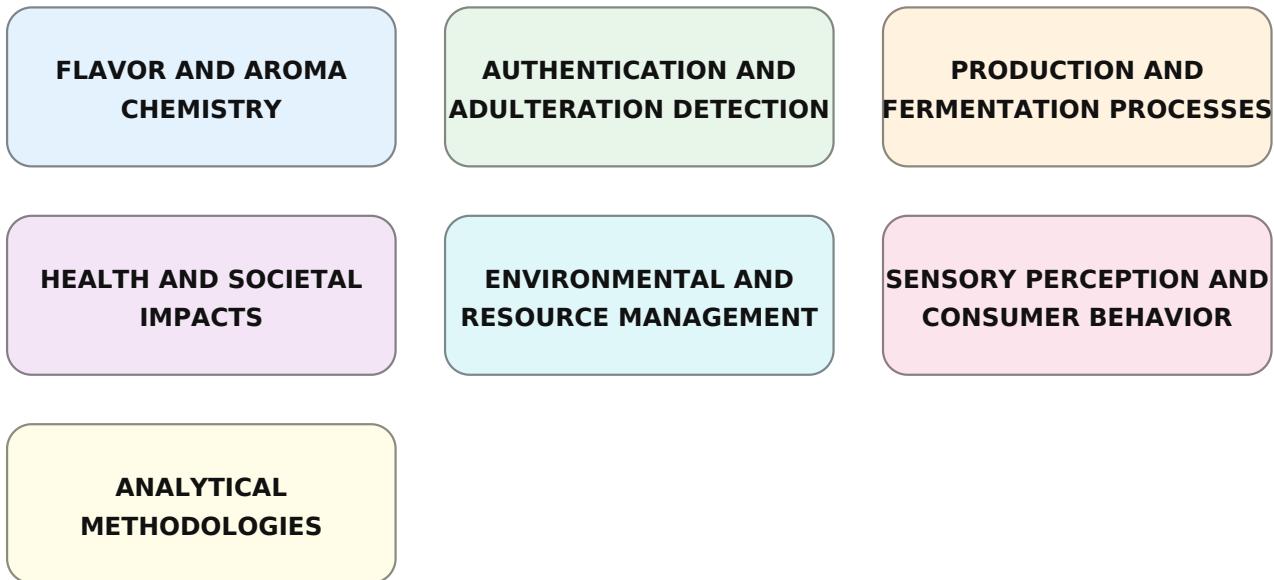


Figure 5. Limitations of current studies (topics)



Figure 6. Future research directions (topics)

