Supplementary materials

Efficacy of mouth rinses and nasal spray in the inactivation of SARS-CoV-2: A systematic review and meta-analysis of *in vitro* and *in vivo* studies

Supplementary Table S1: PRISMA 2020 main checklist

Topic	No.	Item	Location where item is reported
TITLE		Efficacy of mouth rinses and nasal spray in the inactivation of SARS-CoV-2: A systematic review and meta-analysis of in vitro and in vivo studies	
Title	1	Identify the report as a systematic review.	abstract
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist	Supplementary Table 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction and 2.2. Focused questions (Materials and Methods)
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	2.3. Eligibility criteria (Materials and Methods)

Topic	No.	Item	Location where item is reported
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	2.4. Search strategy and data extraction (Materials and Methods)
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary Table 3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	2.4. Search strategy and data extraction (Materials and Methods)
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	2.4. Search strategy and data extraction (Materials and Methods)
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	2.4. Search strategy and data extraction (Materials and Methods)
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	2.4. Search strategy and data extraction (Materials and Methods)

Topic	No.	Item	Location where item is reported
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	2.5. Risk of bias assessment (Materials and Methods)
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	2.6. Data analysis (Materials and Methods)
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item 5)).	2.4. Search strategy and data extraction (Materials and Methods)
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	2.4. Search strategy and data extraction (Materials and Methods)
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	2.4. Search strategy and data extraction (Materials and Methods)
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	2.6. Data analysis (Materials and Methods)
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	2.6. Data analysis (Materials and Methods)
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Materials and Methods

Topic	No.	Item	Location where item is reported
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	2.5. Risk of bias assessment (Materials and Methods)
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Materials and Methods
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	3.1. Results of database searches
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Supplementary Table 6
Study characteristics	17	Cite each included study and present its characteristics.	3.2. General characteristics of the included studies AND Supplementary Tables 4 and 5
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary Tables 7 and 8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplementary Tables 4 and 5
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	3.3. and 3.4. (Results)

Topic	No.	Item	Location where item is reported
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	3.3. and 3.4. (Results)
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Results
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Results
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	3.2. General characteristics of the included studies (Results)
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Results
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion
	23b	Discuss any limitations of the evidence included in the review.	Discussion
	23c	Discuss any limitations of the review processes used.	Discussion
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	2.1. Protocol and registration (Materials and Methods)

Topic	No.	Item	Location where item is reported
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	2.1. Protocol and registration (Materials and Methods)
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Financial support
Competing interests	26	Declare any competing interests of review authors.	Conflicts of Interest
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	All materials are publicly available

Supplementary Table S2: PRIMSA 2020 Abstract Checklist

Topic	No.	Item	Reported?
TITLE		Efficacy of mouth rinses and nasal spray in the inactivation of SARS-CoV-2: A systematic review and meta-analysis of in vitro and in vivo studies	
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			

Topic	No.	Item	Reported?
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

Supplementary Table S3: MeSH terms used for searching through Pubmed, Scopus, Embase Ovid, and Web of Science databases

Platform	MeSH terms
PubMed	((SARS CoV 2[Title/Abstract] OR SARSCoV2[Title/Abstract] OR SARS-CoV2[Title/Abstract] OR Coronavirus[Title/Abstract] OR Corona[Title/Abstract] OR COVID-19[Title/Abstract] OR COVID 19[Title/Abstract] OR cov2[Title/Abstract] OR Acute Respiratory Syndrome Coronavirus 2[Title/Abstract] OR 2019nCoV[Title/Abstract] OR ncov19[Title/Abstract] OR 2019-novel CoV[Title/Abstract]) AND (Mouth wash[Title/Abstract] OR mouthwash[Title/Abstract] OR oral wash[Title/Abstract] OR mouth rinse[Title/Abstract] OR oral rinse[Title/Abstract] OR spray[Title/Abstract] OR nasal spray[Title/Abstract])) AND (English[Language])
Scopus	(TITLE-ABS-KEY (sars AND cov 2 OR sarscov2 OR sars-cov2 OR coronavirus OR corona OR covid-19 OR covid 19 OR cov2 OR acute AND respiratory AND syndrome AND coronavirus 2 OR 2019ncov OR ncov19 OR 2019-novel AND cov) AND TITLE-ABS-KEY (mouth AND wash OR mouthwash OR oral AND wash OR mouth AND rinse OR oral AND rinse OR spray OR nasal AND spray) AND LANGUAGE (english))
Embase Ovid	((SARS CoV 2 or SARSCoV2 or SARS-CoV2 or Coronavirus or Corona or COVID-19 or COVID 19 or cov2 or Acute Respiratory Syndrome Coronavirus 2 or 2019nCoV or ncov19 or 2019-novel CoV) and (Mouth wash or mouthwash or oral wash or mouth rinse or oral rinse or spray or nasal spray)).ab.
Web of Science	(((AB=(SARS CoV 2 OR SARSCoV2 OR SARS-CoV2 OR Coronavirus OR Corona OR COVID-19 OR COVID 19 OR cov2 OR Acute Respiratory Syndrome Coronavirus 2 OR 2019nCoV OR ncov19 OR 2019-novel CoV)) AND AB=(Mouth wash OR mouthwash OR oral wash OR mouth rinse OR oral rinse OR spray OR nasal spray))) AND DOP=(2019-12-01/2022-04-15)

Supplementary Table S4: General descriptions of the included *in vivo* studies and their primary findings.

Study (year)	Country	Active ingredients / concentration	Route	N	values	Main results
Carrouel *et al*. 2021[1]	France	CDCM	Mouth rinse	76	log_{10} copies/ mL	Using CDCM significantly reduced the salivary viral load for at least 4 hours. For long term effects after washing with CDCM once a day for 7 days, CDCM reduced the salivary viral load but not significantly.
Costa *et al*. 2021[2]	Brazil	CHX 0.12%	Mouth rinse	50	Ct	CHX significantly reduced the viral load for up to 60 minutes in comparison to a control group
Eduardo *et al*. 2021[3]	Brazil	CHX	Mouth rinse	8	Ct	Rinsing with CHX or with CPC+Zn significantly reduced the viral load for up to 60 minutes, while HP mouth rinse was associated with a significant reduction for 30 minutes.
		CHX + HP	Mouth rinse	11		
		HP	Mouth rinse	6		
		CPC+ Zn	Mouth rinse	7		
Elzein *et al*. 2021[4]	Lebanon	CHX 0.2%	Mouth rinse	27	Ct	Both CHX and PVP-I showed a significant reduction in the viral load, $p < 0.0001$. However, the mean difference of Ct values in the paired samples was higher for CHX in comparison to PVP-I, 5.69 and 4.45, respectively.
		PVP-I 1.0%	Mouth rinse	25		
Gottsauner *et al*. 2020[5]	Germany	HP 1.0%	Mouth rinse	10	Copies/ mL	Using HP 1.0% reduced the mean value of viral load from 1.8×10^3 to 1.5×10^3 copies/ mL, however, this reduction was not significant.
Guimarães *et al*. 2021[6]	Brazil	HP 1.5%	Mouth rinse	12	Copies/ µL	None of the preparations showed a significant difference in the viral load in comparison to a placebo group. However, HP 1.5% was associated with a significant reduction in the viral load after 30 minutes in comparison to the basal measurements.
		CHX 0.12%	Mouth rinse	12		
		NaClO 0.1%	Mouth rinse	12		
		CHX (0.12%) + HP (1.5%)	Mouth rinse	12		
Lamas *et al*. 2020[7]	Spain	PVP-I 1.0%	Mouth rinse	4	log_{10} copies/ mL	Using PVP-I 1.0% was associated with a significant reduction in the salivary viral load that remained for at least 3 hours.
	Singapore	PVP-I 0.5%	Mouth rinse	4	Ct	

Seneviratne *et al*. 2021[8]		CHX 0.2%	Mouth rinse	6		No statistical differences were found in the Ct values for all preparations. However, both PVP-I 0.5% and CPC showed significant differences in the viral load at certain time points in comparison to water.
		CPC	Mouth rinse	4		
Schürmann *et al*. 2021[9]	Germany	Linola sept,	Mouth rinse	29	Ct	A significant reduction in viral load was reported. The difference in the mean value of Ct was 3.1, which indicated a 90% reduction in the viral load in the pharynx.
Yoon et al. 2020[10]	Korea	CHX 0.12%	Mouth rinse	2	log_{10} copies/ mL	Viral dynamics in various body fluids were checked. The viral load was the highest in the nasopharynx and saliva in comparison to the oropharynx, sputum, and urine. The salivary viral load decreased for 2 hours after CHX rinsing but increased again at 2-4 hours.
Zarabanda *et al*. 2021[11]	USA	PVP-I 0.5%	Nasal spray	11	Ct	A significant reduction in viral load was reported. The mean difference of Ct values was higher for PVP-I 0.5% in comparison to PVP-I 2.0%, - 0.349 and – 1.059, respectively.
		PVP-I 2.0%	Nasal spray	11		
N; the number of subjects, CDCM; b-cyclodextrinecitrox mouthwash, Ct; cycle threshold in qPCR assays, CHX; chlorhexidine, HP; hydrogen peroxide, CPC; cetylpyridinium chloride, Zn; Zinc, PVP-I; povidone-iodine, NaClO; sodium hypochlorite, Linola sept; Linola sept, Dr. August Wolff GmbH (commercial name).						

Supplementary Table S5: General descriptions of the included *in vitro* studies and their primary findings (all preparations are mouth rinse unless otherwise specified)

Study	Active ingredients / concentrations	Methods	Major findings
Anderson *et al*. 2020[12]	(PVP-I 0.5%), (PVP-I 1.0%)	SARS-CoV-2 (hCoV19/ Singapore/2/2020) was cultivated in Vero-E6 cells. The virus was exposed to the test products at 21°C for 30 seconds. Experiments were carried out in triplicates.	All test products showed a ≥ 4 LRV of the virus titres, which is corresponding to 99.99%.
Anderson *et al*. 2022[13]	(CPC 0.07% + herbs extracts), (CPC 0.07%), (CHX 0.2%)	SARS-CoV-2 (USA-WA1/2020) in Vero E6 cells. The virus was exposed to the test products for 30 seconds at room temperature. Tests were performed in triplicates.	CPC preparations were associated with ≥ 4 LRV of the virus titres, while CHX showed < 2.0 LRV.
Bidra *et al*. (1) 2020[14]	(PVP-1 1.5%), (PVP-1 0.75%), (PVP-1 0.5%), (EtOH 70%)	SARS-CoV-2 (USA-WA1/2020) was propagated in Vero 76 cells. The virus was exposed to the test products at room temperature for 15 and 30 seconds. Experiments were carried out in triplicates.	The LRVs for all PVP-I preparations were 3.0 at 15 seconds and 3.33 at 30 seconds. EtOH 70% was associated with an LRV of 2.17 at 15 seconds and 3.33 at 30 seconds.
Bidra (2) *et al*. 2020[15]	(PVP-I 0.5%), (PVP-I 1.25%), (PVP-I 1.5%), (HP 1.5%), (HP 3.0%)	SARS-CoV-2 (USA-WA1/2020) in Vero 76 cells. The virus was exposed to the test products at room temperature for 15 and 30 seconds. Experiments were carried out in triplicates.	PVP-I preparations were associated with >4.33 LRVs at 15 seconds and >3.63 LRV at 30 seconds. The LRVs for HP 1.5% at 15 and 30 seconds were 1.33 and 1.0, respectively. The LRVs for HP 3.0% at 15 and 30 seconds were 1.0 and 1.8, respectively.
Davies *et al*. 2021[16]	(CHX 0.2%), (CHX 0.2% + EtOH), (Listerine Advanced®: dipotassium oxalate 1.4%), (Listerine Total Care®: NaF, ZnF_2, menthol, thymol), (HClO 0.01-0.02%),	SARS-CoV-2 England 2 strain propagated in Vero E6 cells. The virus was exposed to the test products at room temperature for 60 seconds. All products were tested in triplicates.	The highest LRV (≥ 5.5) was associated with HClO and followed by PVP-I and Listerine Total Care® (≥ 4.1). The LRV of Listerine Advanced® was ≥ 3.5. Other products associated with LRVs ≤ 0.5.

	(HP 1.5%), (PVP-I 0.58%)		
Frank *et al*. 2020a[17]	(PVP-I 2.5%), (PVP-I 1.25%), (PVP-I 0.5%) (All were nasal sprays)	SARS-CoV-2 (USA-WA1/2020) strain was grown in Vero 76 cells. The test solutions and the virus were incubated at room temperature for 15 and 30 seconds. Each concentration was tested in triplicate.	The LRVs for all test products were 3.0 when incubated for 15 seconds and 3.33 when incubated for 30 seconds.
Gudmundsdottir *et al* 2020[18]	(Mouth spray ColdZyme®: glycerol, trypsin, EtOH <1%)	SARS-CoV-2 (USA-WA1/2020) strain was grown in Vero 76 cells. Tests were done in duplicate.	The tested product was associated with LRV = 1.76, which is equivalent to the inactivation of 98.3% of virus titres.
Hassandarvish *et al*. 2020[19]	(PVP-I 0.5%), (PVP-I 1.0%)	SARS-CoV-2 (SARS-COV-2/ MY/ UM/6-3) cultivated in Vero E6 cells. Virus inactivation tests were performed under clean and dirty conditions for 15, 30, and 60 seconds. Dirty conditions were stimulated by adding human erythrocytes to simulate organic soiling.	PVP-I 1.0% was associated with LRVs > 5 for all time frames. The LRVs were > 4 for PVP-I 0.5% at 15 seconds and > 5 at 30 and 60 seconds. LRVs were not changed between the clean and dirty conditions.
Kariwa *et al*. 2020[20]	(PVP-I 0.23%), (PVP-I 0.35%), (PVP-I 0.45%)	SARS-CoV-2 (WK-521 strain) was propagated in Vero E6 cells. The virus was exposed to the test products for 30 and 60 seconds.	All preparations were associated with LRVs > 3.1. This is corresponding to inactivation of > 99.92.
Koch-Heier *et al*. 2021[21]	(HP 1.5% + CPC 0.05%), (CHX 0.1% + CPC 0.05%), (CHX 0.1% + CPC 0.05%), (CHX 0.1%), (HP 1.5%), (CPC 0.05%)	SARS-CoV-2; Isolate "FI-100" was propagated in Vero E6 cells. The virus was exposed to test products for 30 seconds at 37°C. Each product was tested in duplicates.	The highest LRVs were reported for HP 1.5% + CPC 0.05% and CHX 0.1% + CPC 0.05% (LRV ≥1.9). CHX 0.1% + CPC 0.05% and CPC 0.05% were associated with LRVs equal 1.2 and 0.7, respectively. Other test products did not show reduction in the virus titre.
Komine *et al*. 2021[22]	(CHX 0.06% + CPC 0.05%), (CHX 0.12% + CPC 0.05%), (CPC 0.075% CHX 0.12%),	SARS-CoV-2 (JPN/TY/WK-521 strain) was propagated in Vero E6 cells. The virus was incubated with the test products at 25°C for 20, 30, and 180 seconds. All experiments were performed in triplicates.	All the products containing CPC inactivated the virus between 3.3 to > 4.4 LRV. The LRV associated with Del hydrochloride was > 5.4. A test product with only CHX did not show sufficient inactivation capacity against the virus, LRV = 0.2.

	(Del hydrochloride, CPC 0.05%)		
Kontos 2021[23]	(essential iodine drops 50%), (essential iodine drops 66%), (essential iodine drops 75%)	SARS-CoV-2 (USA-WA1/2020) in Vero 76 cells. Test products were tested in triplicates at room temperature for 60 and 90 seconds.	At 60 seconds, the concentrations of 66% and 75% were associated with LRVs equal to 1.7 and 2.0, respectively. The LRV of the 50% concentration was 2.0 for 90 seconds.
Liang *et al*. 2020[24]	(PVP-I 0.9%), (PVP-I 0.5%), (PVP-I 0.28%), (PVP-I 0.09%), (PVP-I 0.54%), (PVP-I 0.3%), (PVP-I 0.17%), (PVP-I 0.05%)	SARS-CoV-2 (USA-WA1/2020) was propagated in Vero 76 cells. The virus was incubated with the tested concentrations at 37°C for 30 seconds, 2, and 10 minutes. All experiments were performed in triplicates.	The concentrations ≥ 0.3% were associated with LRVs ≥ 3.1 for 30 seconds. Other concentrations associated with LRVs ranged between 1.2 to 2.2 for 30 seconds. Increasing the exposure time did not increase the LRVs.
Meister *et al*. 2022[25]	(0.4mg/ml $NaClO_2$), ($NaClO_2$ 0.9%, panthenol), (dexpanthenol 50 mg/mL), ($NaClO_2$<0.08%, Xylometazolin hydrochloride 0.1%), (disodium succinate)	SARS-CoV-2 (hCoV-19/ Germany/BY-Bochum-1/2020) cultivated in Vero E6 cells. The virus was inactivated by the test products for 30 seconds. All experiments were performed in triplicates.	Only Sodium hypochlorite ($NaClO_2$ <0.05%) lowered the viral titres by 2.21. The LRVs for all other products ranged from 0.18 to 0.53.
Pelletier *et al*. 2021[26]	(nasal spray PVP-I 2.5%), (nasal spray PVP-I 1.25%),	SARS-CoV-2 (USA-WA1/2020) was grown in Vero 76 cells. The virus was incubated with the test products for 60 seconds at room temperature. All products were tested in triplicates.	The LRVs for all tested products were 4.63 at 60 seconds.

	(nasal spray PVP-I 0.5%), (PVP-I 1.5%), (PVP-I 0.75%), (PVP-I 0.5%)		
Pyrć *et al*. 2021[27]	(GCPQ molecular weight=10kDa), (GCPQ molecular weight=30kDa), (GCPQ molecular weight=15kDa), (GCPQ molecular weight=60kDa)	SARS-CoV-2 (isolate 026 V-03883) was propagated in Vero E6 cells and A549 cells. All tests were carried out in triplicates.	The highest LRVs were associated with molecular weights 10kDa and 15kDa, 3.87 and 1.79, respectively. The LRVs of the other preparations were ≤ 0.24.
Santos *et al*. 2021[28]	(Mouth rinse 0.1% APD), (Dental gel 1.0% APD)	Samples of SARS-CoV-2 were collected from oropharyngeal samples and propagated in Vero CCL-81 cells. The virus was inactivated with the tested products for 30. 60, and 300 seconds.	The mouth rinse was associated with LRV = 4.5, corresponding to 99.99% of viral inactivation. The dental gel showed lower efficiency with LRV = equals 1.5, corresponding to 90% of viral inactivation.
Shet *et al*. 2022[29]	(PVP-I 0.5%)	SARS-CoV-2 (USA-WA1/2020) in Vero 76 cells. The virus was inactivated by the test product at room temperature for 15, 30, 60, and 300 seconds. The experiment was repeated in triplicates.	The LRV was > 4 at 30 and 300 seconds. At 15 and 60 seconds, the LRVs were 2.8 and 3.67, respectively.
Shewale *et al*. 2021[30]	All products are commercially from CloSYS: Toothpaste, (NaF 0.24%, Sensitive Mouthwash ClO_2, Na_3PO_4, citric acid), (Ultra-Sensitive Mouthwash	SARS-CoV-2 (USA-WA1/2020) in Vero E6 cells. The virus was inactivated by the test products 30, 60 and/or 120 seconds at room temperature.	The toothpaste was associated with LRV = 2.26 for 30, 60, and 120 seconds, which is equivalent to the inactivation of 99.4% of the virus. The sensitive mouthwash showed LRV equals 1.81 and 1.71 at 30 and 60 seconds, respectively, which is corresponding to the inactivation of≥ 98% of the virus. The LRVs for the ultra-sensitive mouthwash were 1.96 at 30 seconds and 1.39 at 60 seconds, which is corresponding to the inactivation of 98.4% and 96.3% of the virus, respectively. Finally, The oral spray was associated with LRV equals 2.98 at 30 seconds and 2.67 at 60 seconds, which is

	ClO_2, Na_3PO_4, citric acid), (Oral Spray ClO_2, Na_3PO_4, citric acid)		corresponding to the inactivation of 99.9% and 99.7% of the virus, respectively.
Steinhauer *et al*. 2021[31]	(CHX 0.1%), (CHX 0.2%)	SARS-CoV-2 was inactivated by the tested products for 1 to 10 minutes. The experiments were repeated in duplicates.	The concertation of 0.1% was associated with LRV <1 at 10 minutes while the 0.2% was associated with LRV <1 at 1 and 5 minutes.
Teagle *et al.* 2022[32]	(Molecular iodine)	SARS-CoV-2 (USA-WA1/2020) was propagated in Vero E6 cells. The virus was inactivated by the tested product with/without the presence of saliva for 30 and 60 seconds.	The LRV was 4.75 at 30 seconds and ≥5.25 at 60 seconds with the presence of saliva. Without saliva, the LRV was ≥5.75 at 30 and 60 seconds. The reported LRVs are equivalent to inactivation of >99.99% of virus.
Tiong *et al*. 2021[33]	(CHX 0.12%), (CPC 0.075%+ NaF 0.05%), (thymol 0.05%), (Hexetidine 0.1%+EtOH 9%, NaCl 2% 0.4M)	SARS-CoV-2 was isolated from a nasopharyngeal/oropharyngeal swap sample (SARS-COV-2/MY/UM/6-3; TIDREC) of a positive individual and propagated in Vero E6 cells. The virus was inactivated by the test products under 2 conditions, clean and dirty (by adding human erythrocytes) for a period of 30 and 60 seconds.	CHX preparation was associated with LRV = 4 for 30 and 60 seconds under dirty and clean conditions. CPC and hexetidine preparations showed LRVs equal to 5 for 30 and 60 seconds and under all conditions. Under the clean condition, thymol preparation was associated with LRV = 0.5 at 30 seconds and LRV = 0.75 at 60 seconds. For the dirty condition, the LRV for the thymol preparation was 0.5 at 30 and 60 seconds.
PVP-I; povidone-iodine, CPC; cetylpyridinium chloride, CHX; chlorhexidine, EtOH; ethanol, HP; hydrogen peroxide, SDS; sodium dodecyl sulfate, NaF; sodium fluoride, ZnF_2; zinc difluoride, HClO; hypochlorous acid, $NaClO_2$; sodium chlorite, GCPQ; a polymer name (N-palmitoyl-N-monomethyl-N,N-dimethyl-N,N,N-trimethyl-6-O-glycolchitosan), ADP; anionic phthalocyanine derivate, ClO_2; chlorine dioxide, Na_3PO_4; trisodium phosphate, NaCl; sodium chloride.			

Supplementary Table S6: Excluded studies and reasons of exclusion

Study	Reason of exclusion
Abdelalim et al. (2021) [34] **Chaudhary et al. (2021)**[35] **Burgos-Ramos et al. (2022)**[36] **Orcina et al. (2021)**[37] **Di Domênico et al. (2021)**[38] **Figueroa et al. (2021)**[39] **Guenezan et al. (2021)**[40] **Huang and Huang (2021)**[41] **Kasiri et al. (2021)**[42] **Arefin et al. (2021)**[43] **Khan et al. (2020)**[44] **Saud et al. (2022)**[45] **Avhad et al. (2020)**[46] **Almanza-Reyes et al. (2021)**[47] **Aref et al. (2021)**[48]	Subject-level reports of SARS-CoV-2 viral load was not mentioned
Laferl et al. (2022)[49] **Michel et al. (2021)**[50] **Mora-Aguilera (2022)**[51]	Papers for diagnostic rather than therapeutic purposes
Paull et al. (2021)[52] **Errecalde et al. (2021)**[53]	*In vivo* animal study
Jain et al. (2021)[54]	The number of replicates is not mentioned
Bañó-Polo et al. (2022)[55] **Bansal et al. (2021)**[56] **Bentley et al. (2021)**[57] **Bovard et al. (2022)**[58] **Haridas et al. (2021)**[59] **Moakes et al. (2021)**[60] **Morokutti-Kurz et al (2021)**[61]	LRV between control and experimental groups is not mentioned

Muñoz-Basagoiti et al (2021)[62] **Paolacci et al. (2021)[63]** **Rodriguez et al. (2021)[64]** **Sharad and Kapur (2021)[65]** **Tateyama-Makino et al. (2021)[66]** **Yadalam et al. (2021)[67]** **Casanovas et al. (2021)[68]** **Robinson et al. (2021)[69]**	
Westover et al. (2020)[70] **Cannon et al. (2020)[71]** **Mohamed et al. (2020)[72]** **Statkute et al. (2020)[73]** **Xu et al. (2021)[74]**	High Contact time (incompatible with EN 14476:2013+A2:2019), not peer reviewed
Buonavoglia et al. (2021)[75] **Green et al. (2020)[76]** **Shet et al. (2021)[77]**	Used of SARS-CoV-2 surrogates
Balouch et al. (2021)[78] **Frank et al. (2020b)[79]** **Vergara-Buenaventura and Castro-Ruiz (2020)[80]** **Telles-Araujo et al. (2020)[81]** **Gerlach et al. (2020)[82]** **Carrouel et al. (2020)[83]** **Peng et al. (2020)[84]** **Pattanshetty et al. (2021)[85]**	Not experimental, expert opinions, or commentaries

Supplementary Table S7: Risk of bias assessment of *in vivo* studies

Study	ToxRTool items, *in vivo* (0 = no, 1 = yes)															Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	
Carrouel et al. 2021[1]	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	**14**
Costa et al. 2021[2]	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	**13**
Eduardo et al. 2021[3]	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	**13**
Elzein et al. 2021[4]	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	**12**
Gottsauner et al. 2020[5]	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	**12**
Guimarães et al. 2021[6]	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	**12**
Lamas et al. 2020[7]	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	**12**
Seneviratne et al. 2021[8]	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	**13**
Schürmann et al. 2021[9]	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	**14**
Yoon et al. 2020[10]	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	**13**
Zarabanda et al. 2021[11]	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	**13**

Legend for Supplementary Table S7:

The Risk of Bias Assessment for *in vivo* studies was done using the Toxicological data reliability assessment tool (ToxRTool, *in vivo* part). The following are the questions that were used for this purpose:

1. Was the test substance identified?
2. Was the purity/concentration of the substance given?
3. Was the information on the source/origin of the substance given?
4. Was the virus strain (a strain of SARS-CoV-2) given?
5. Was the administration route given?

6. Were frequency and duration of exposure as well as time-points of observations explained?
7. Were negative (where required) and positive controls (where required) included?
8. Was the number of subjects per group given?
9. Were the study endpoint(s) and their method(s) of determination clearly described?
10. Were sufficient details of the administration scheme given to judge the study?
11. Was the description of the study results for all endpoints investigated transparent and complete?
12. Were the statistical methods applied for data analysis given and applied in a transparent manner?
13. Was the study design chosen appropriately for obtaining the substance-specific data aimed at?
14. Were the quantitative study results reliable?
15. Were used primers, probes, and standard errors, explained clearly?

Supplementary Table S8: Risk of bias assessment of *in vitro* studies

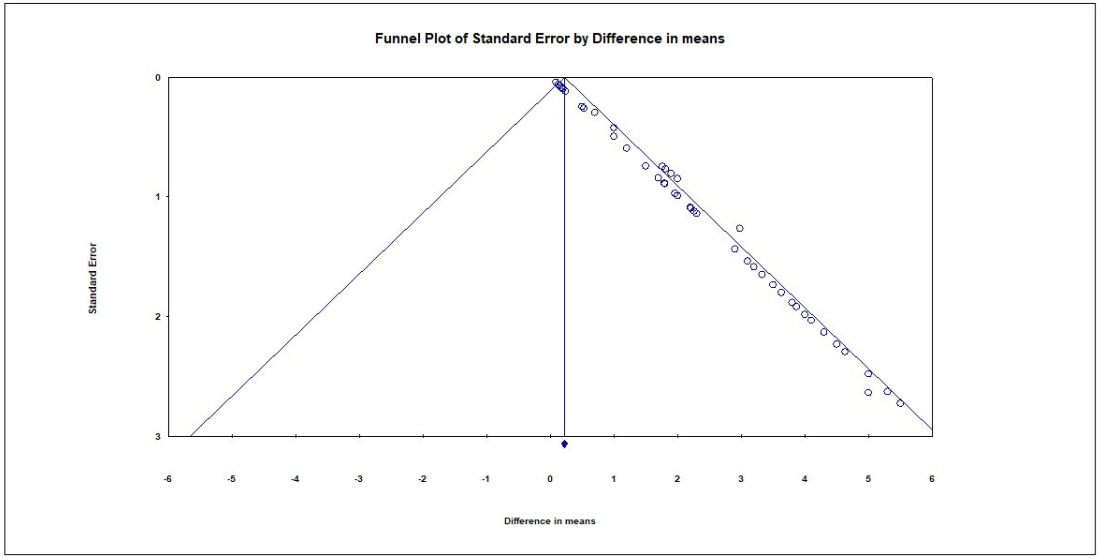
Study	ToxRTool items, *in vitro* (0 = no, 1 = yes)																	Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	
Anderson *et al.* 2020[12]	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	**17**
Anderson *et al.* 2022[13]	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	**16**
Bidra *et al*. (1) 2020[14]	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	**16**
Bidra (2*) et al*. 2020[15]	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	**16**
Davies *et al.* 2021[16]	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	**15**
Frank et al. 2020a[17]	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	**16**
Gudmundsdottir *et al.* 2020[18]	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	**16**
Hassandarvish *et al.* 2020[19]	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	**15**
Kariwa *et al*. 2020[20]	1	1	0	1	1	0	1	1	1	1	0	1	1	1	1	1	1	**14**
Koch-Heier *et al.* 2021[21]	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	**16**
Komine *et al*. 2021[22]	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	**17**
Kontos 2021[23]	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	**17**
Liang *et al*. 2020[24]	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	**16**
Meister *et al*. 2022[25]	1	1	0	1	1	0	1	1	1	1	0	1	1	1	1	1	1	**15**
Pelletier *et al*. 2021[26]	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	**16**
Pyrć *et al*. 2021[27]	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	**15**
Santos *et al*. 2021[28]	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	**17**
Shet *et al*. 2022[29]	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	**16**
Shewale *et al*. 2021[30]	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	**16**
Steinhauer *et al.* 2021[31]	1	1	1	1	1	0	0	1	1	1	0	1	1	1	1	1	1	**15**
Teagle *et al.* 2022[32]	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	**16**
Tiong *et al*. 2021[33]	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	**15**

Legend for Supplementary Table S8:

The Risk of Bias Assessment for *in vitro* studies was done using the Toxicological data reliability assessment tool (ToxRTool, *in vitro* part). The following are the questions that were used for this purpose:

1. Was the test substance identified?
2. Was the purity/concentration of the substance given?
3. Was the information on the source/origin of the substance given?
4. Was the test system described (type of cells or tissue used: primary cells, cell lines)?
5. Was the strain of SARS-CoV-2 given?
6. Was information given on the source/origin of the test system (laboratory/scientist/company providing cell lines)?
7. Was necessary information on test system properties, and conditions of cultivation and maintenance given?
8. Was the method of administration given?
9. Were frequency and duration of exposure as well as time-points of observations explained?
10. Were negative controls included?
11. Were positive controls included?
12. Was the number of replicates (or complete repetitions of the experiment) given?
13. Were the study endpoint(s) and their method(s) of determination clearly described?
14. Was the description of the study results for all endpoints investigated transparent and complete?
15. Were doses administered or concentrations in application media given?
16. Was the study design chosen appropriately for obtaining the substance-specific data aimed at?
17. Are the quantitative study results reliable?

Supplementary Figure S1: Funnel plot of the standard error by difference in means for *in vitro* studies



Model		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	79	0.220	0.025	0.001	0.171	0.268	8.885	0.000	253.179	78	0.000	69.192	0.127	0.072	0.005	0.356
Random effects	79	0.886	0.089	0.008	0.712	1.060	9.982	0.000								

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