



Philippine COVID-19 Living Clinical Practice Guidelines

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EVIDENCE SUMMARY

Should copper-containing masks be used to decrease SARS-CoV-2 transmission?

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RECOMMENDATION

There is no evidence to recommend the use of copper-containing over non-copper-containing masks to decrease SARS-CoV-2 transmission.

Consensus Issues

Due to the absence of clinical trials on the efficacy of copper-containing masks in reducing COVID-19 transmission, the panel members opted to have no recommendation. One panelist voted against the use of copper masks because of the higher costs compared with using surgical or cloth masks and the potential harm of metal leaching from copper-containing textiles.

Key Findings

Currently, there are no clinical trials directly comparing copper-containing masks with non-copper-containing masks in terms of SARS-CoV-2 transmission. There are no clinical trials directly comparing copper-containing masks with non-copper-containing masks in terms of SARS-CoV-2 transmission, except in two in-vitro studies. One study demonstrated the metal leaching potential of copper-containing textiles could potentially lead to adverse events attributed to inhalation or ingestion of copper. In terms of cost, copper-containing masks are more expensive than regular masks.

Introduction

SARS-CoV-2, the causative agent of COVID-19, is an enveloped single-stranded RNA virus of the Coronaviridae family.[1] It is mainly transmitted through respiratory droplets which can be spread by infected persons as they breathe, talk, cough, or sneeze. The wearing of face masks reduces this transmission by blocking exhaled droplets of infected persons as well as preventing inhalation of droplets by those who are not infected. To put it simply, it provides a physical barrier between the virus and uninfected individuals.[2] To further improve the efficacy of these face masks, manufacturers sought to apply a chemical barrier which would inactivate the virus as it passes through the material. Copper, an anti-microbial chemical used in clinical settings, was the most popular choice.[1] Though its mechanism of action against viruses is not yet fully understood, it is theorized that it inactivates proteases necessary for viral replication.[3] In earlier studies on SARS-CoV, MERS-CoV, HCoV, and different strains of influenza, various forms of copper were shown to inhibit, inactivate, and destroy the viruses within minutes. It was hypothesized that copper-containing masks would be as effective against SARS-CoV-2.[1] This review aims to determine the efficacy and safety of copper masks in decreasing SARS-CoV transmission.



Review Methods

We searched the Cochrane Library, PubMed, MEDLINE, Google Scholar, JSTOR, HERDIN, WHO ICTRP and ClinicalTrials.gov using a combined MeSH and free text search with the terms “SARS-CoV-2”, “COVID-19”, “virus”, “viral”, “viral load”, “copper”, “Cu”, “mask”, “face mask”, “infused”, “coated”, “containing”, “filter”, “transmission”, “transmissibility”, and “inactivation”. The study characteristics that were searched for were: Population – people without COVID-19/suspected to be at risk for COVID-19; Intervention – copper-containing masks; Comparator – non-copper-containing masks; Outcomes – viral load, adverse events. Randomized controlled trials were prioritized in the search. When none were found, non-randomized and observational studies were screened as well. When systematic reviews or meta-analyses were found, the individual studies were assessed for possible inclusion.

Results

As of this date, there are no randomized controlled trials on the use of copper-containing masks against SARS-CoV-2 transmission. There were two in-vitro studies which tested for the anti-viral capabilities of copper-containing masks.

One study used real-time polymerase chain reaction (RT-PCR) and immunochemical staining to detect SARS-CoV-2 in exposed Vero cells protected with either regular KF94 masks or copper-coated [75% cuprous oxide (Cu_2O), 25% cupric oxide (CuO)] KF94 masks. A SARS-CoV-2-containing medium was applied to the copper-coated and non-coated materials for one hour. Viruses extracted from the different materials were then transferred to Vero cells. A separate group of Vero cells were directly infected with the viral medium to serve as the control. Fluorescent images were acquired using an automated microscope, and image analysis using proprietary software was done to quantify the nucleocapsid expression. After 36 hours, there was a 75% decrease in fluorescence in the copper-coated group; after 48 hours, RT-PCR did not detect SARS-CoV-2 genes in the same group. Meanwhile, the non-coated group showed similar results with the control group.[4]

Another study used microscopy, immunofluorescence assay, and RT-PCR on exposed Vero cells to compare the efficacy of mixed-fiber (nylon, polyester, spandex) masks and three-layer copper sulfide (CuS)-impregnated masks. Discs of the copper-containing cloth and the non-copper-containing cloth were transferred to plates which were then exposed to a SARS-CoV-2 suspension. The different plate groups were incubated for 30 minutes, 1 hour, and 2 hours. Afterwards, the discs were washed with a clean medium. The collected fluids were then used to infect Vero cell plates which were incubated for 1 hour. Cell plates directly inoculated with SARS-CoV-2 were used as a control group. Fluorescence was completely absent in the copper-containing cloth group for all incubation periods while the non-copper-containing cloth group showed similar results with the control group. Similarly, RT-PCR showed a remarkable decrease in viral copy numbers in the copper-containing cloth group for all incubation periods. The same study tested different concentrations of CuS (5%, 10%, 15%, 20%) directly inoculated in a SARS-CoV-2 medium. The resulting suspensions were incubated for 30 minutes, 1 hour, and 2 hours, after which the extracted supernatants were used to infect Vero cells for 1 hour. The observed fluorescence and viral copy numbers were found to be inversely proportional to the concentration of the CuS solution used.[5]

One safety issue found was the potential for metal leaching from copper-containing textiles. The study of Pollard et al. on different antimicrobial fabrics showed that copper was more susceptible to leaching at higher concentrations. This increased the possibility of inhalation or ingestion of copper which can lead to headache, vertigo, respiratory irritation, hepatomegaly, and other



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gastrointestinal issues.[6] For dermatologic effects, however, copper-containing cloths were found to have low risk of causing adverse skin reactions.[7]

Evidence to Decision

There were no cost-effectiveness studies on copper-containing masks found during the literature search. In the Philippines, surgical masks usually cost about ₱120 for a box of 50 pieces (~₱2.4/mask) and regular cloth masks cost approximately ₱50-₱300 per mask depending on the material. Copper-containing masks, whether branded or not, are generally more expensive at around ₱140-₱980 per mask.[8]

Mask Type	Cost per piece
Copper Mask	₱140-₱980
Cloth Mask	₱50-₱300
Surgical Mask (Polypropylene)	₱2.4

Recommendations from Other Groups

Currently, there are no recommendations from medical organizations regarding the use of copper-containing masks against SARS-CoV-2 transmission. The Department of Health stated that copper-containing masks provide a physical barrier from droplets, which is similar to how regular masks offer protection. However, it also warns against using advertised copper masks with holes or slits as they allow unfiltered air flow.[9]

Research Gaps

From the article search, there are currently no ongoing trials on copper-containing masks registered on HERDIN, on the WHO International Clinical Trials Registry Platform, or on *ClinicalTrials.gov*. Studies have yet to be conducted which address the benefits and harms of copper-containing masks on human participants.



References

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Appendix 1. Evidence to Decision

Table 1. Summary of initial judgments prior to the actual panel meeting (n = 11)

FACTORS	JUDGMENT					RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS FROM PANEL MEMBERS	
	No (3)	Yes (8)					
Problem	No (3)	Yes (8)					
Benefits	Large (2)	Moderate (3)	Small (4)	Uncertain (2)			<ul style="list-style-type: none"> Reduced detected SARS-CoV-2 in Vero cells by 75%
Harm	Large (6)	Small (2)	Uncertain (3)	Varies			<ul style="list-style-type: none"> Copper have the potential to leach and can be inhaled, ingested or absorbed by wearer Consider the adverse effect of copper mask related to prolonged use; alcohol-based hand rub cannot be used for hand hygiene after touching the copper part; needs soap and water.
Certainty of Evidence	High	Moderate	Low	Very low (11)			<ul style="list-style-type: none"> None
Balance of effects	Favors copper mask	Does not favor copper mask (2)	Uncertain (9)	Varies			<ul style="list-style-type: none"> In vitro studies showed that copper masks can reduce the detected and inhibit replication of SARS-CoV-2 but they have the potential to leach. Copper can be inhaled, ingested or absorbed by wearer.
Values	Important uncertainty or variability	Possibly important uncertainty or variability (3)	Possibly NO important uncertainty or variability (5)	No important uncertainty or variability (3)			<ul style="list-style-type: none"> No clinical trial on effectiveness of copper mask in reducing SARS-CoV-2 transmission
Resources Required	Uncertain	Large cost (9)	Moderate Cost (2)	Negligible cost	Moderate savings	Large savings	<ul style="list-style-type: none"> Copper mask: Php 140 – Php 980 Surgical masks: Php 120 per box of 50 pcs (Php 2.4/pc) or cloth mask: Php50—300 depending on material
Certainty of evidence of	No included studies	Very low (2)	Low (1)	Moderate	High (1)		<ul style="list-style-type: none"> No research evidence found.



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FACTORS		JUDGMENT				RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS FROM PANEL MEMBERS
required resources	(7)					
Cost effectiveness	No included studies (9)	Favors the comparison (1)	Does not favor either the intervention or the comparison (1)	Favors the intervention		<ul style="list-style-type: none"> No research evidence found.
Equity	Uncertain (8)	Reduced (2)	Probably no impact	Increased (1)		<ul style="list-style-type: none"> No research evidence found.
Acceptability	Uncertain (7)	No (3)	Yes (1)	Varies		<ul style="list-style-type: none"> No research evidence found.
Feasibility	Uncertain (8)	No (2)	Yes (1)	Varies		



Appendix 2. Search Yield and Results

1. Summary

#	Query	Results
1	"copper" OR "Cu"	6,064,719
2	"infused" OR "coated" OR "containing" OR "filter"	9,208,873
3	"mask" OR "face mask"	3,967,523
4	"SARS-CoV-2" OR "COVID-19"	170,721
5	"virus" OR "viral"	5,397,143
6	"transmission" OR "transmissibility"	6,252,741
7	"inactivation"	2,655,892
8	"viral load"	1,224,058
9	#1 AND #2	4,015,788
10	#3 AND #9	403,351
11	#4 AND #5	79,774
12	#5 AND #7	1,297,515
13	#6 AND #11	32,657
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	2,504

2. Cochrane Library

#	Query	Results
1	"copper" OR "Cu"	4296
2	"infused" OR "coated" OR "containing" OR "filter"	71383
3	"mask" OR "face mask"	11260
4	"SARS-CoV-2" OR "COVID-19"	2
5	"virus" OR "viral"	46151
6	"transmission" OR "transmissibility"	11479
7	"inactivation"	3072
8	"viral load"	6703
9	#1 AND #2	531
10	#3 AND #9	28
11	#4 AND #5	2
12	#5 AND #7	249
13	#6 AND #11	0
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	0

3. PubMed

#	Query	Results
1	"copper" OR "Cu"	19,587
2	"infused" OR "coated" OR "containing" OR "filter"	115,235
3	"mask" OR "face mask"	5,795
4	"SARS-CoV-2" OR "COVID-19"	137,106
5	"virus" OR "viral"	174,454
6	"transmission" OR "transmissibility"	80,954
7	"inactivation"	13,102



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8	"viral load"	9,249
9	#1 AND #2	2,150
10	#3 AND #9	8
11	#4 AND #5	58,489
12	#5 AND #7	1,284
13	#6 AND #11	10,275
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	1

4. MEDLINE

#	Query	Results
1	"copper" OR "Cu"	8,120
2	"infused" OR "coated" OR "containing" OR "filter"	19,222
3	"mask" OR "face mask"	3,985
4	"SARS-CoV-2" OR "COVID-19"	3,303
5	"virus" OR "viral"	14,642
6	"transmission" OR "transmissibility"	10,926
7	"inactivation"	476
8	"viral load"	257
9	#1 AND #2	5,173
10	#3 AND #9	1,452
11	#4 AND #5	469
12	#5 AND #7	111
13	#6 AND #11	932
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	1

5. Google Scholar

#	Query	Results
1	"copper" OR "Cu"	5,490,000
2	"infused" OR "coated" OR "containing" OR "filter"	7,460,000
3	"mask" OR "face mask"	3,780,000
4	"SARS-CoV-2" OR "COVID-19"	17,800
5	"virus" OR "viral"	4,900,000
6	"transmission" OR "transmissibility"	5,690,000
7	"inactivation"	2,590,000
8	"viral load"	1,200,000
9	#1 AND #2	3,830,000
10	#3 AND #9	395,000
11	#4 AND #5	17,900
12	#5 AND #7	1,280,000
13	#6 AND #11	20,100
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	2,500



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6. JSTOR

#	Query	Results
1	"copper" OR "Cu"	541,781
2	"infused" OR "coated" OR "containing" OR "filter"	1,524,422
3	"mask" OR "face mask"	164,268
4	"SARS-CoV-2" OR "COVID-19"	2,268
5	"virus" OR "viral"	251,567
6	"transmission" OR "transmissibility"	457,879
7	"inactivation"	49,169
8	"viral load"	7,274
9	#1 AND #2	177,665
10	#3 AND #9	6,834
11	#4 AND #5	717
12	#5 AND #7	14,667
13	#6 AND #11	1,350
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	2

7. HERDIN

#	Query	Results
1	"copper" OR "Cu"	93
2	"infused" OR "coated" OR "containing" OR "filter"	216
3	"mask" OR "face mask"	47
4	"SARS-CoV-2" OR "COVID-19"	81
5	"virus" OR "viral"	1178
6	"transmission" OR "transmissibility"	579
7	"inactivation"	15
8	"viral load"	209
9	#1 AND #2	216
10	#3 AND #9	28
11	#4 AND #5	1178
12	#5 AND #7	1191
13	#6 AND #11	0
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	0

8. WHO ICTRP

#	Query	Results
1	"copper" OR "Cu"	842
2	"infused" OR "coated" OR "containing" OR "filter"	18,395
3	"mask" OR "face mask"	2,168
4	"SARS-CoV-2" OR "COVID-19"	10,161
5	"virus" OR "viral"	9,151
6	"transmission" OR "transmissibility"	924
7	"inactivation"	58
8	"viral load"	366
9	#1 AND #2	53



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10	#3 AND #9	1
11	#4 AND #5	1,019
12	#5 AND #7	13
13	#6 AND #11	0
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	0

Appendix 3. Characteristics of Included Studies

Study ID	Patients (n)	Interventions	Outcomes	Method
Jung 2021	None	75% cuprous oxide (Cu ₂ O) and 25% cupric oxide (CuO) coated KF94 face masks	SARS-CoV-2 infection of Vero cells	In Vitro Study
Hewawaduge 2021	None	three-layer copper sulfide (CuS) impregnated face masks	SARS-CoV-2 infection of Vero cells SARS-CoV-2 replication	In Vitro Study