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Efficacy of Potassium Aluminum Sulfate $(KAlSO_4)_2$ and Povidone Iodine $(C_6H_9I_2NO)$ as Crede's Prophylaxis against *Ophthalmia Neonatorum*

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ABSTRACTS

Neonatal conjunctivitis is a worldwide problem. Although global incidence is not known, incidents of 1-24% have been reported from various regions of the world especially those practicing home delivery without standard prophylaxis. This study was an in-vitro investigation on possible prophylaxis for ophthalmia neonatorum (ON) like potassium aluminum sulfate $(KAlSO_4)_2$ and povidone iodine $(C_6H_9I_2NO)$ in comparison to tetracycline. A five by three (5x3) factorial experiment in Completely Randomized Design (CRD) was used in this study. Factor A was the five-test bacteria, namely *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Enterobacter spp*. and *Pseudomonas spp*. while Factor B was the experimental variables or the substances to be tested such as alum, povidone iodine and tetracycline. Aluminum was diluted and subjected to purity test prior to bacteria assay. The zone of inhibition was measured using a caliper and results were recorded. Based on the in-vitro analysis, aluminum showed a positive response to the five tested bacteria as it yielded a comparative mean results of

growth inhibition. Among the possible applications of the findings in the study could be the formulation of antiseptic eye drops with the use of alum or Povidone iodine to be used as prophylaxis to guard against neonatal conjunctivitis.

Keywords **—** Health science, in-vitro investigation, zone of inhibitions, prophylactic agents, ophthalmia neonatorum, Philippines

INTRODUCTION

Based on the reports from various regions of the world, ophthalmia neonatorum has recorded 1-24% of incidences making it one among top global health problems. Most the epidemiological findings are related to gonococcal and chlamydial ON because it is related to sexually-transmitted diseases and are, therefore, of general public health importance. In this case, expectant women are the main source of infection that is reason that neonates born to such mothers have a high risk of contracting the disease during delivery. The occurrence of ON is associated to socioeconomic status of the area like in United States of America which ranges from 1% to 2%.

Neonatal conjunctivitis or ophthalmia neonatorum (ON), is a commonly encountered problem which presents during the first month of life. The causes can be septic or aseptic and the majority of infectious neonatal conjunctivitis are of bacterial etiology. In spite most of these cases are benign, some of them may progress to systemic complications or visual loss if left untreated. Often, but not invariably, bacterial conjunctivitis has a longer incubation period as compared to other infective causes. Clinical signs include redness, tearing, secretion, conjunctival and palpebral inflammation, a pseudo membrane and corneal perforation which may result in blindness.

Ocular prophylaxis is still warranted because not all women receive prenatal care, and, therefore, not all women are able to be diagnosed prenatally (Mabry-Hernandez, & Oliverio-Hoffman, 2010). It is a common knowledge in the Philippines that home delivery conducted by a *comadrona* or *hilot* is still a usual practice especially in the rural areas. In such cases, no standard prophylaxis is used to guard against neonatal conjunctivitis. From this standpoint, it is deemed significant by the researcher to conduct an in-vitro investigation on possible remedies for the prevention of neonatal conjunctivitis. It is sought by the proponent to determine alternative agents like alum and Povidone iodine in comparison to tetracycline which is the current drug choice for Crede's Prophylaxis. With

the rising cost of medicines and hospitalization, babies delivered at home might be spared from neonatal conjunctivitis through the discovery of safe, affordable indigenous alternatives to the current drug choice.

This study also aimed to determine whether alum or potassium aluminum sulfate can be used to substitute tetracycline which is the current prophylactic drug choice for neonatal conjunctivitis. This is for the reason that based on research findings, cases of neonatal conjunctivitis still occur in spite of treatment with tetracycline. The same is true in the case of Povidone iodine, a commonly-used antiseptic. Alum is inexpensive and very easily available in the market, even in far-flung rural areas. It is a common household remedy for body odor and mouth sores or thrush or "singaw." It is claimed by the researcher from personal experience and observation that alum quite readily relieves and heals said sores.

OBJECTIVES OF THE STUDY

The study was conducted to determine safe, effective, and inexpensive possible alternative prophylactic agent in vitro for ON that can be used as home remedy for home-delivered babies.

Specifically, it sought: 1) To determine the antibacterial property of potassium aluminum sulfate, povidone iodine and tetracycline at 5% concentration in vitro against the following test bacteria: *Staphylococcus aureus*, *Escherichia coli, Klebsiella pneumoniae*, *Enterobacter spp.* and *Pseudomonas spp.* in terms of zone of growth inhibition; 2) To measure zone of growth inhibitions of potassium aluminum sulfate, povidone iodine and tetracycline at 5% concentration against the test bacteria namely *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter spp.* and *Pseudomonas spp.*; 3) To compare zone of growth inhibitions of potassium aluminum sulfate, povidone iodine and tetracycline at 5% concentration against the test bacteria namely *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Enterobacter spp.* and *Pseudomonas spp.*; and 4) To determine and compare the periods of first growth inhibitions of potassium aluminum sulfate, povidone iodine and tetracycline at 5% concentration against test bacteria namely *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Enterobacter spp.* and *Pseudomonas spp.*

MATERIALS AND METHODS

A five by three (5x3) factorial experiment in Completely Randomized Design (CRD) was used in this study. Factor A was the five-test bacteria, namely

Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Enterobacter spp. and Pseudomonas spp. while Factor B was the experimental variables or the substances to be tested such as alum, povidone iodine and tetracycline. The different combination was presented in Table C while the set-ups were as follows:

Factor A (Test Bacteria)

A1 *Staphylococcus aureus*
A2 *Escherichia coli*
A3 *Klebsiella pneumoniae*
A4 *Enterobacter spp.*
A5 *Pseudomonas spp.*

Factor B (Experimental Prophylactic Agents)

B1 5% Potassium Aluminum Sulfate
B2 5% Povidone Iodine
B3 5% Tetracycline

Table 1. Experimental set-ups used in the study

TEST BACTERIA (A)	PROPHYLACTIC AGENTS (B)		
	B1	**B2**	**B3**
A1	A1B1	A1B2	A1B3
A2	A2B1	A2B2	A2B3
A3	A3B1	A3B2	A3B3
A4	A4B1	A4B2	A4B3
A5	A5B1	A5B2	A5B3

The five bacterial strains were purchased from Luna Goco Medical Center. The bacteria sensitivity test started by bringing Mueller Hinton agar, Tetracycline antibiotic, blank discs and bacterial strains to room temperature. In a sterile tube, 1 ml of 5 % Povidone-iodine and 1 ml of 5 % alum were transferred in a separate tube. The five blank discs were soaked to each solution of Povidone-iodine and alum for 30 minutes. Five sterile tubes were prepared and each tube was labelled with respective bacterial strains. The 2.5 ml of normal saline solution was transferred in each tube for preparation of bacterial suspension.

The tube was heated before and after transferring of sample or inocula. The inoculating needle was heated. Using the inoculating needle, a single colony

of each bacteria was picked and was emulsified with NSS in each respective tubes. The suspension was mixed. A sterile cotton swab was submerged in each prepared bacterial suspension. The cotton tip was allowed to absorb the suspension for some time. Then, the Mueller Hinton agar was labelled with the name of bacteria, alum, Povidone-iodine and Tetracycline. Each suspension was swabbed in Mueller Hinton agar using overlapping streak technique. The streaked suspension was allowed to dry. A pre-soaked disc in each solution of Povidone-iodine and alum was planted respectively to the Mueller Hinton agar with specified bacteria. Tetracycline was also planted to each respective plate to serve as control. The plates were incubated in 35-37 degree Celsius for 18-24 hours. Each plate was examined after 8 hours for initial growth and final growth after 24 hours. Lastly, the zone of inhibition was measured using a caliper and results were recorded.

Standard laboratory precautions in handling pathogenic bacteria were observed throughout the experiment.

Data collected were analyzed using GLM Procedure of the Analysis of Variance (ANOVA) of the two factorial Completely Randomized Design (CRD). Mean comparison for the significant differences among treatment combination means was further analyzed using Duncan's Multiple Range Test (DMRT) at 1% and 5% level of significance.

RESULTS AND DISCUSSION

Antibacterial property of alum, povidone iodine and tetracycline

The antibacterial property of alum, povidone iodine and tetracycline against the five test bacteria namely: *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Enterobacter spp.* and *Pseudomonas spp* was presented in Table 2.

It is significant to note that both alum and povidone iodine inhibit the growth of test bacteria. Relative to the result, alum recorded the highest growth inhibition against *S. aureus* with 27 mm. In addition, it also shows positive response against *E.coli, and Pseudomonas* spp. for recording both 23 mm growth inhibitions. For *Enterobacter spp.* and *K. pneumoniae,* equally 20 mm growth inhibition was recorded.

Whereas, a 19 mm growth inhibition was the highest recorded for povidone iodine against *S. aureus.* against *E. coli* and *Enterobacter*, both 12 mm zone of inhibition was recorded. For *K. pneumonia,* 11 mm growth inhibition was recorded and for *Pseudomonas spp.,* 8 mm growth inhibition was recorded.

For tetracycline, results reveal that *S. aureus* had the highest growth inhibition of 29 mm while both *E. coli* and *Enterobacter* gained 25 mm. 22 mm growth inhibition was recorded for *K. pneumoniae*, and 14 mm for *Pseudomonas spp.*

Findings indicate that all the three substances tested, namely, alum, povidone iodine and tetracycline effectively inhibited the growth of the test bacteria: *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Enterobacter spp.* and *Pseudomonas spp.* in the experiment within the trial period of twenty-four hours.

Results show a possibility that alum might be proven to be effective as a prophylaxis for ophthalmia neonatorum in the future after further studies that need to be conducted. Animal studies could later be conducted to test for possible adverse reactions *in vivo*. Mucous membranes like the surface coverings of the eyes are quite delicate.

Table 2. Antibacterial property of alum, povidone iodine and tetracycline against test bacteria

Test Bacteria	Mean Growth Inhibitions of Substances Tested (mm)		
	Experimental		Control
	Alum (B1)	Povidone-iodine (B2)	Tetracycline (B3)
S. aureus (A1)	27 mm	19 mm	29 mm
E. coli (A2)	23 mm	12 mm	25 mm
K. pneumoniae (A3	20 mm	11 mm	22 mm
Enterobacter spp.(A4)	20 mm	12 mm	25 mm
Pseudomonas spp. (A5)	23 mm	8 mm	14 mm

Zone of growth inhibitions as affected by five-test bacteria

Test bacteria

The zone of inhibition against the five test bacteria at 5 % concentration of the prophylactic agents was recorded and was presented in Table 3. Analysis showed that the growth of inhibitions is highly significantly different ($P<0.01$).

Results show that the highest zone of inhibition among the five test bacterial agent of ophthalmia neonatorum was observed in *S. aureus* with a mean 24.33 mm. It is significant to note that among the five test bacteria, *S. aureus* was the most vulnerable or defenseless against the three prophylactic agents. Having a consistent result for *S. aureus*, it suggests that the three prophylactic agents were effective in inhibiting the growth of the bacteria.

On the other hand, *E.coli, K. pneumoniae* and *Enterobacter spp.* showed a comparable (P<0.05) effect to the three prophylactic agents. As revealed in Table 3, *E. coli* recorded 19.09 mm inhibition, *K. pnuemoniae* with 17.86 mm and for *Enterobacter* of 18. 67 mm growth. This verifies that the three bacteria were also susceptible to be inhibited by the prophylactic agents next to *S. aureus*.

On the contrary, *Pseudomonas spp.* showed an outstanding resistance among the five test bacteria against the three prophylactic agents. It was revealed that only 13. 56 mm growth inhibition was recorded for *Pseudomonas spp. a*mong the five test bacteria. Although relatively low in terms of growth inhibition, it still verifies that the three prophylactic agents did show an effect or positive response to the bacteria.

The result of *Pseudomonas spp.* as the most resistant among the five test bacteria can be attributed to the report of Van Duin and Paterson (2016) in a Medical Journal relative to antibiotic resistance that *Pseudomonas spp.* is a Gram-negative bacteria and are multi-drug resistant (MDR).

However, *S. aureus* along with other test bacteria may develop resistance to tetracycline due to sustained use of it (Speer, Shoemaker, & Salyers, 1992).

Furthermore, the results of the five test bacteria can be correlated to Matejcek and Goldman (2013) that emergence of neonatal conjunctivitis are caused by the said bacterial agents.

Table 3. Zone of growth inhibitions as affected by the test bacteria

FACTOR A-Test Bacteria	ZONE OF GROWTH INHIBITION (mm)
S. aureus (A1)	24.33[a]
E. coli (A2)	19.09[b]
Klebsiella pneumoniae (A3)	17.86[b]
Enterobacter spp. (A4)	18.67[b]
Pseudomonas spp. (A5)	13.56[c]

Legend: *Means within column with different superscript are significantly different (P<0.01)*

Prophylactic agents

The effect of alum, povidone iodine and tetracycline against test bacteria *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Enterobacter spp.* and *Pseudomonas spp*. is reflected in Table 4. Results showed a significant difference (P<0.01) in the effect of the three prophylactic agents against the five test bacteria.

Moreover, the growth of inhibition against the five test bacteria recorded in the tetracycline is significantly higher (P<0.01) compared to the growth of

inhibitions of povidone iodine but are comparable (P<0.05) to the growth inhibitions observed and measured in alum. Tetracycline which is the current drug of choice for prophylaxis against neonatal conjunctivitis and as the experimental control showed an outstanding effect for having recorded a mean of 21.60 mm growth inhibition against the five test bacteria.

This clarifies that using tetracycline to the five test bacteria is effective but this result does not coincide with the article *"Treatment and prevention of ophthalmia neonatorum"* (Matejcek, & Goldman,2013) having 10% to 20% failure rate and some infants required a second or occasionally intervention of other prophylactic agents. Despite the long use of tetracycline as prophylactic agent for neonatal conjunctivitis, there is still an emergence and recurrence of the bacterial neonatal conjunctivitis which coincides with the findings of Rasool *et al.* (2016) that bacterial isolates are now 64.6 % resistant to tetracycline.

On the other hand, povidone iodine which is also a common antiseptic but is not used for the eyes before but currently being utilized preoperatively as an antiseptic in eye surgeries was tested against *S. aureus, E.coli, K pneumoniae, Enterobacter spp.* and *Pseudomonas spp.* to investigate whether it can be used as an alternative to Crede's prophylaxis.

This outcome confirms the conclusions of Simon (2003) that povidone iodine when used to neonates as prophylactic agents reappeared more commonly in the first 3 days after treatment with povidone iodine. This also proves that Povidone iodine is associated with noninfective (sterile) conjunctivitis, probably because of its toxicity to the ocular surface in neonates.

In case of alum as prophylactic agent, a mean of 21.60 mm growth inhibitions was recorded which is comparable (P<0.05) to 22.60 mm growth inhibition of tetracycline. Among the five test bacteria, alum showed a consistent effect of mean growth inhibition, meaning, it can be a possible substitute for Crede's prophylaxis.

Table 4. Zone of growth inhibition as affected prophylactic agents

FACTOR B Prophylactic Agent	ZONE OF INHIBITION (mm)
Alum (B1)	21.60[a]
Povidone iodine (B2)	12.00[b]
Tetracycline (B3)	22.67[a]

Legend: *Means within column with different superscript are significantly different (P<0.01)*

Comparison of growth inhibitions of alum, povidone iodine and tetracycline at 5% concentration against the test bacteria

The comparison of the mean growth inhibitions of alum, povidone iodine and tetracycline against *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Enterobacter spp.* and *Pseudomonas spp*. is revealed in Table 5. Results showed significant (P<0.01) interaction effect of the five test bacteria and three prophylactic agents.The findings show that the tetracycline shows a consistent effect to the four bacteria, however, alum shows significant (P<0.01) positive effect on *Pseudomonas spp*. having 19.33 mm growth inhibitions compared to 13.67 mm of tetracycline. On the other hand, tetracycline recorded the highest growth inhibition against *S. aureus* with a mean of 28. 67 mm which is comparable (P<0.05) with alum having a growth inhibition of 26.67 mm.

This also reveals the comparison between potassium aluminum sulfate and povidone iodine against the five test bacteria, namely, *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Enterobacter spp.* and *Pseudomonas spp*. Based on the table, the highest mean growth inhibition for povidone iodine was recorded to *S. aureus* with a mean 17.67 mm which is relatively low compared to a mean of 26.67 mm inhibition in alum.

This result gains support in the study of*Speer et al.* (1992) that although tetracycline and povidone iodine showed a pronounced effect to the bacterial agents, still the occurrence and reappearance of the bacterial infection recurs in a period of three to four days. This maybe because that bacterial agents are becoming resistant to the consistent use of tetracycline and povidone iodine.

Another study confirms the result of this study that *Pseudomonas spp*. having the lowest inhibition is a multi-drug resistant bacteria along with other gram positive and gram negative bacteria (Van Duin & Paterson, 2017).

Table 5. Zone of inhibition as affected by the interaction of test bacteria and prophylactic agents

TEST BACTERIA	SUBSTANCE TESTED		
	Alum (B1)	Povidone iodine (B2)	Tetracycline (B3)
S. aureus (A1)	26.67[a]	17.67[b]	28.67[a]
E. coli (A2)	22.67[a]	11.50[b]	24.00[a]
K. pneumoniae (A3)	19.67[a]	11.50[b]	21.50[a]
Enterobacter spp. (A4)	19.67[a]	11.67[b]	24.67[a]
Pseudomonas spp. (A5)	19.33[a]	7.6[c]	13.67[b]

Legend — *Means within rows with different superscript are significantly different (P<0.01)*

Periods of first growth inhibitions of alum, povidone iodine and tetracycline at 5% concentration against test bacteria

The periods of first growth inhibitions of alum, povidone iodine and tetracycline at 5% concentration against test bacterianamely *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Enterobacter spp.* and *Pseudomonas spp.* was presented in Table 6. Results showed that tetracycline posted an outstanding effect and fastest rate ($P<0.05$) of showing growth inhibitions after 8 hours of incubation against the five test bacteria.

However, povidone iodine also shows positive inhibitory effects after 8 hours of incubation for *S. aureus.* against *E. coli, K. pneumoniae* and *Enterobacter spp.*, zone of growth inhibition was observed after 12 hours and the latest was 16 hours of incubation. For alum, the earliest observed zone of inhibition was recorded after 12 hours of incubation against *S. aureus, K. pnuemoniae and Pseudomonas spp.* against *Enterobacter spp.* zone of growth inhibition was recorded after 16 hours and the latest was 20 hours of incubation against *E. coli.*

Results can be correlated to the findings of the study entitled, "*Tetracycline Antibiotics: Mode of Action, Applications, Molecular Biology, and Epidemiology of Bacterial Resistance"* (Chopra & Roberts, 2001) that tetracycline exhibited activity against a wide range of microorganisms including gram-positive and gram-negative bacteria, chlamydiae, mycoplasmas, rickettsia, and protozoan parasites for the 8 hours period of incubation but then it was discovered earlier in 1940's and its continued use resulted to antibiotic resistance at about 64.6% (Dagnachew, 2014). However, alum was tested for antibacterial activity and was proven to inhibit growth of bacteria but since this study was the pioneer in the field of ophthalmic application, it may be a good a substitute since this is foreign to different bacterial agents.

Table 6. Periods of first growth inhibitions of alum, povidone iodine and tetracycline at 5% concentration against test bacteria

Test Bacteria	Period of First Growth Inhibitions of Substances Tested (hrs)		
	Experimental		Control
	Alum (B1)	Povidone-iodine (B2)	Tetracycline (B3)
S. aureus (A1)	12 hrs[a]	8 hrs[b]	8 hrs[b]
E. coli (A2)	20 hrs[a]	12 hrs[b]	8 hrs[b]
K. pneumonia (A3	12 hrs[a]	12 hrs[a]	8 hrs[a]

Enterobacter spp. (A4)	16 hrs[a]	12 hrs[b]	8 hrs[b]
Pseudomonas spp. (A5)	12hrs[b]	16 hrs[a]	8 hrs[b]

Legend: *Means within rows with different superscripts are significantly different (P<0.05)*

CONCLUSIONS

Based on the in-vitro analysis, potassium aluminum sulfate can be used as prophylaxis against Pseudomonas spp., a bacterial agent of ophthalmia neonatorum. Since it outperformed tetracycline and has comparable effect with tetracycline against *S. aureus, E. coli, K. pneumonia* and *Enterobacter spp*.

Potassium aluminum sulfate showed a positive response to the five test bacteria as it yielded a comparative mean results of growth inhibition. Still povidone iodine manifests a good effect but not comparable to potassium aluminum sulfate and tetracycline.

Tetracycline showed a consistent effect to the five bacteria, however, potassium aluminum sulfate showed a positive effect on *Pseudomonas spp*. in terms of its rate of first period of growth inhibition. Although tetracycline showed better compared to potassium aluminum sulfate and povidone iodine but then still potassium aluminum sulfate and povidone iodine manifested positive activity against the test bacteria.

Tetracycline showed the fastest effect compared to the two substances tested which potassium aluminum sulfate and povidone iodine; however, potassium aluminum sulfate and povidone iodine still showed a positive response to the test bacteria.

TRANSLATIONAL RESEARCH

Potassium aluminum sulfate commonly known as *tawas* can be used as substitute prophylaxis to tetracycline and also a potent antibacterial agent against *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Enterobacter spp*. and *Pseudomonas spp*. based on the bacterial assay administered. On this note, considering that the results are highly favorable, an awareness campaign or information dissemination through extension activity of the institution maybe conducted for this reason. On the other hand, the college school paper may write a feature article discussing the beneficial results of this study. Since the target clienteles of this project is to help indigenous people when it comes to health and sanitation, a literacy or health forum maybe conducted relative to this

study. Other prints like brochures, leaflets and manuals or broadcast media may be considered to better educate the people regarding the use and benefits of the present research results.

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