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Formulation and Antimicrobial Evaluation of Isopropyl Hand Sanitizer using Co-processed Excipients

O. D. AKIN-AJANI*[A-F], T. O. AJALA[A-B, E-F], M. A. OGUNNUBI[B]

Department of Pharmaceutics & Industrial Pharmacy, University of Ibadan, Ibadan, Nigeria

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article.

Abstract

Background: In response to the Ebola virus outbreak in West Africa in the year 2014, which caused the Ebola haemorrhagic fever, the WHO alcohol-based hand rub formulation was adopted in addition to regular hand washing to prevent the spread. However, other formulation factors rather than alcohol concentration alone can greatly influence the overall antimicrobial efficacy of hand disinfectants.

Objective: To formulate an antimicrobial hand sanitizer using co-processed carriers.

Methodology: Carbopol (F), HPMC (G) and co-processed forms of both polymers in batches- 1:1(A), 1:2(B), 1:4(C), 2:1(D) and 4:1(E) respectively were used. The polymers were characterized, and used as carriers in formulating hand sanitizers (A to G). The formulated hand sanitizers were evaluated for physical appearance, pH, clarity, viscosity, drying time and antimicrobial activity, in comparison to a commercially available hand sanitizer (CAHS).

Results: Co-processing significantly ($p<0.05$) improved both hydration capacity of carbopol and viscosity of HPMC. The physical appearance, pH and opacity were maintained throughout the study. All the formulations showed dilatant rheological behaviour while the CAHS exhibited plastic flow. The drying times for the formulated hand sanitizers were comparable to CAHS but longer than isopropyl alcohol implying prolonged action at application site. The antimicrobial activity of the formulations was of the rank order isopropyl alcohol>B>F>CAHS>D>E>C>G>A.

Conclusion: Co-processing of excipients improved the pharmaceutical properties of the hand sanitizers with antimicrobial activity that was comparable to CAHS but lower than isopropyl alcohol. The hand sanitizer formulated with polymer batch B, demonstrated optimum antimicrobial and pharmaceutical properties and may be developed for commercial use.

Keywords: Hand sanitizer formulation, Isopropyl alcohol, Carbopol, Hydroxypropyl MethylCellulose, Co-processed excipient.

INTRODUCTION

The Ebola virus, which is characterized with haemorrhagic fever, caused an epidemic in 2014, and subsequently spread from Guinea to other West African Countries such as Sierra Leone, Liberia, Nigeria, Senegal, and Mali. The virus was transmitted from wild animals to humans (WHO, 2016). The spread of the virus from the infected human population to the uninfected human was by close contact. This implies that the secretions, mucous membrane with blood, organs or other body fluid of the infected person

as well as any surface or material that had been contaminated with these fluids, could infect an uninfected person with broken skin. One of the suggested methods by the World Health Organization (WHO) in preventing the spread of the virus was by reduction of human-to-human transmission amongst others, which could be achieved by regular hand washing (WHO, 2016). However, since the soap and liquid required for the hand washing could not be carried about, there was the need to formulate a preparation, which would work effectively as the soap and water, if not better and would be mobile. Foddai *et al.* (2016) compared the efficacy of hand sanitizers with water and soap and concluded that alcohol-based products achieved rapid and effective inactivation of various bacteria than water and soap. The result was the WHO alcohol-based hand rub formulation that was fast acting; effective, well tolerated and which also improved hand hygiene (WHO, 2010). The "recipe" of two different formulations that were made available included an isopropyl based hand rub and an ethanol-based hand rub, along with emollients to protect hands and a specific ingredient that will eliminate spore from components of the reused bottle. Although Nigeria has been declared free from Ebola virus transmission in October 2014 (Reliefweb, 2014), Nigerians still need to adhere to the knowledge of proper hand hygiene by using hand rub or hand sanitizers for improvement of hygiene and general disease prevention.

The probability of transmission increases when personal hygiene or hand washing habits are inadequate or compromised (Lubrizol, 2009). Germs are sometimes contacted in hospital settings, or obtained from a simple handshake, touching of common objects in public areas and or answering a phone. There is potential exposure to an array of harmful and potentially infectious bacteria and viruses whether travelling by air, road or rail, as well as visiting public places in general (Cosmeticskenya, 2015). It has been found that product formulation can greatly influence the overall antimicrobial efficacy of hand disinfectants and is a more important factor than alcohol concentration alone (Edmonds *et al*., 2012). Alcohol alone leads to whitening of the hands caused by excessive skin dryness, which is not aesthetic.

Carbopol and HPMC are polymers useful as excipients in the formulation of both liquid and solid dosage forms. In liquid dosage forms, these polymers act as thickening agents, prevent settling/sedimentation of suspended solids, modify viscosity, which could assist in moistening of the hands, and generally act by entrapping solid particles in the solution (Chaudhari and Patil, 2012). Carbopol has very high viscosity but does not hydrate easily and lumps may be formed during production if extra caution is not taken. Our preliminary study showed that carbopol hydrated after 24 h. Hydroxypropyl methylcellulose (HPMC), on the other hand, is almost freely soluble and much less viscous than carbopol. Co-processing of these polymers will lead to new and functional carriers for the active agent in hand sanitizer formulation. It is expected that the co-processed polymers will have lower hydration time that would enable faster processing and improve the properties of the formulations. There are several methods of co-processing, each with its merits and demerits. Co-grinding, is a co-processing method termed physical modification and has the advantages of being simple, economical and time-saving in comparison to chemical, crystallization and other forms of alteration (Ahuja *et al*., 2015). The aim of the study, therefore, was to formulate antimicrobial hand sanitizers using co-processed carriers – carbopol and hydroxypropyl methylcellulose (HPMC) - that will ensure a drying time that will prevent whitening of the hands.

METHODOLOGY

Materials

The materials used were Carbopol (Lubrizol Corporation, Wickliffe, Ohio, USA) and Hydroxypropyl Methylcellulose, HPMC (Colorcon Ltd, Datford Kent, England), Deionized water, Isopropanol (laboratory grade), Glycerin, Triethanolamine, Fragrance, Colourant, Nutrient Agar

(Biomark Laboratories, India), Sabourad Dextrose Agar (LAB M Ltd, Lancashire, UK), a commercially available hand sanitizer, CAHS, (obtained from a supermarket in Ibadan, Nigeria).

Co-processing of the polymers

The polymer batches were prepared using the co-grinding method with slight modification (Akin-Ajani *et al*., 2018). Equivalent weights of Carbopol and HPMC for polymer batch A were weighed and triturated for 5 min. The co-processed polymer was transferred into a pre-washed, oven dried and air cooled bottle. The bottle was put in a tumbling mixer (Forster Equipment Co. Ltd, Whetstone, Leicester, England) for 15 min. Polymer batch A was then transferred into a labelled container. The procedure was repeated for polymer batches B, C, D and E respectively. The ratio for the polymer batches is shown in Table 1. The polymers were then subjected to FT-IR analysis to confirm that polymers were actually co-processed. The FT-IR spectrometry of the polymers prepared in potassium bromide (KBr) disks was carried out using an FT-IR system (Spectrum BX 273, Perkin–Elmer, USA) with a scanning range of 350–4000 cm^{-1}.

Table 1: **Polymer Ratios used in hand sanitizer production**

Polymer Batch	Carbopol : HPMC ratios
A	1:1
B	1:2
C	1:4
D	2:1
E	4:1
F	Carbopol only
G	HPMC only

Microscopy of the Polymers

Each sample was spread on a glass slide and viewed under a light microscope (Accu-Scope 3012-LED Commack, NY) using a magnification of 40. Photomicrographs were taken with TSView® Software (Tucsen Imaging Technology Co., Ltd. Fujian, China) for imaging. The mean projected diameter (μm) was also determined by measuring the diameters of 100 particles under the microscope.

Determination of Particle Density

The particle density (Pρ) of the polymers was determined by the liquid pycnometer method using xylene as the displacement fluid. A 50 mL pycnometer was weighed empty (W), filled with xylene (non-solvent) and the excess wiped off. The weight of the pycnometer with the non-solvent was determined (W_1). The difference in weight W_1 and W was calculated as (W_2). A 2 g quantity of the sample was weighed (W_3) and quantitatively transferred into the pycnometer bottle. The excess non-solvent was wiped off and the pycnometer was weighed again (W_4). The particle density was calculated from equation 1:

$$P\rho = \frac{W2 \times W3}{50(W3 - W4 + W2 + W)} \qquad (1)$$

Determination of Water Absorption Capacity

The polymer sample (0.5 g) was weighed into a 15 mL centrifuge tube. About 10 mL of distilled water was added in aliquots. It was agitated for 2 min and placed in a centrifuge at 2200 rpm for 20 min. The supernatant was decanted. The residue was transferred into a pre-weighed crucible and weighed again. The weight of the residue was determined (W_1), the absorbed water was removed by drying the residue at 100 °C to a constant weight (W_2) in an oven. The water absorption capacity was then expressed as the weight of water bound by 100 g of each powder sample as:

$$\text{Water Absorption Capacity} = {}^{(W_1 - W_2)}/_{W} \times 100 \qquad (2)$$

Determination of Hydration Period

The polymer (2.5 g) was transferred into a 50 mL beaker. Distilled water (10 mL) was added to it and it was stirred for 5 min. It was allowed to stand for 24 h and was checked for the complete hydration of the polymers. Complete hydration was determined using constant viscosity value of the dispersion.

Determination of viscosity

The viscosity of 2 % ${}^{w}/_{v}$ slurry of the co-polymers were determined after hydrating for 1 h and again at 72 h using the Brookfield viscometer (RVVDV-II + Pro, Brookfield Eng Labs Inc Middle Boro, MA, USA), with spindle size 03 at the shear rate of 0.3, 0.6, 2.5, 5, 10, 20, 30, 50, 60, 100 rpm respectively.

Preparation of the Hand Sanitizers

Hand sanitizers (50 mL batches) were prepared using the formula shown in Table 2. The equivalent weight of the co-processed polymer blend batch was weighed and added to half of the required volume of deionized water. This was triturated quickly to prevent large clumps and kept aside for complete hydration. The remaining volume of the deionized water was added along with the glycerine to the hydrate obtained. Isopropanol was added slowly after which the fragrance was added. The pH of the formulation was adjusted to 7 – 7.5 by adding triethanolamine (TEA). The resulting formulation was a viscous gel with a transparent outlook. The colorant was then added as required.

Table 2. The formula for the Hand Sanitizers

Ingredients	**Concentration ($\%^{w}/_{w}$)**
Deionized water	28.49
Polymer	0.25
Humectant (Glycerine)	0.70
Isopropyl alcohol	70.00
Neutralizer (Triethanolamine)	0.26
Fragrance	0.10
Colorant	0.20

Storage conditions

The formulated hand sanitizers, as well as the CAHS, were kept on a shelf and the temperature and humidity were recorded from an electronic thermometer and hygrometer (OPTILAB Electronic Thermo-Hygrometer, Model THC-20, Wei Jian Electronics, Ltd., China).

Evaluation of the Formulated Hand Sanitizers

Determination of viscosity

Using the Brookfield viscometer (RVVDV-II + Pro, Brookfield Eng. Labs Inc. Middle Boro, MA, USA), the formulated and the CAHS were analysed for viscosity using spindle 03 and 05 respectively at shear rates of 10, 20, 30, 50, 60 and 100. The viscosity of the CAHS was analysed using spindle 05 because it was too viscous for spindle 03.

Measurement of pH

The pH of the formulated sanitizers and CAHS was measured using PHS-3C pH meter (Ningbo Hinotek Technology Co., Ltd, China).

Determination of Clarity

The clarity of the formulated hand sanitizers and CAHS was determined by measuring the transmittance at a wavelength of 420 nm using Spectrum Lab 752S UV spectrophotometer (752S12078, Bicotek Ningbo Ltd., China). The active ingredient used, Isopropyl alcohol was tested for its transmittance to ensure its purity and to avoid contaminants that can cause a reduction in the transmittance.

Determination of the drying time of the formulated hand sanitizers

The drying time of the formulated sanitizers and CAHS were determined by applying the hand sanitizer and rubbing the palms together after which the time taken for complete drying was recorded.

In- vitro antimicrobial activity by agar plate diffusion method (cup plate method)

The required amount of agar for both bacteria (Nutrient Agar) and fungi (Sabouraud Dextrose Agar) were weighed and dissolved in sufficient quantity of distilled water respectively. Each solution was homogenized for 30 min before transferring into separate bijou bottles. Each agar was sterilized in an autoclave (model LS-B5OL-III, ZIRBUS technology, Germany) for 15 min at 121 °C. Distilled water, 9 mL each in six test tubes was also sterilized under the same conditions. Overnight cultures were prepared by transferring 1 mL each of *Staphylococcus aureus, Escherichia coli, Bacillus subtilis, Salmonella typhi, and Candida albicans* into 5 mL broth.

Each organism (1 mL) was withdrawn from the broth and transferred aseptically into the sterilized distilled water. The petri dishes were labelled and the melted agar was transferred aseptically into each of the pre-labelled plates and allowed to set and cool for 1 h. The microorganisms were then lightly and carefully

swabbed on each plate using a cotton swab and left for 15 min. An 8 mm cork borer was used aseptically to bore holes on the plate and the formulated sanitizers and CAHS were dropped into the hole meant for each. The plate was left for 1 h to allow for diffusion of the sanitizers into the agar before incubation. The bacteria isolates were incubated at 37 °C for 24 to 48 h while the fungal isolate was incubated at 25 °C for 72 h. The positive control used for the bacteria was 10 µg/ml gentamicin and for the fungus, 1 % $^{w}/_{v}$ fluconazole.

RESULTS AND DISCUSSION

Polymer Properties

The photomicrographs of the polymers are shown in Figure 1 while the mean projected diameters are presented in Table 3. Polymer batch F had vibrio shaped particles while polymer batch G had a rod to needle-like shaped particles. All the co-processed polymers at different ratios had a mixture of both shapes in different portions.

The FT-IR spectra of Carbopol (F), HPMC (G) and co-processed forms of both polymers in batches- A (1:1), B (1:2), C (1:4), D (2:1) and E (4:1) are presented in Figure 2. The parent polymers had certain discernible absorbance ranging from the O-H (3000-3600 cm^{-1}) stretch characteristic of polysaccharides, and 1641.91 – 1651.28 cm^{-1}, carbonyl group C=O conjugate (Kalita *et al.*, 2014). The FTIR spectra of HPMC showed two characteristic peaks at 942.31 and 2933.00 cm^{-1} while the characteristic peaks of carbopol was obtained at 1437.00 and 1635.46 cm^{-1}. These characteristic peaks of the parent polymers made it possible to identify that co-processing had taken place in the different polymer ratios. The CH stretch (3000 – 2850 cm^{-1}), and O-H bend (950 – 910 cm^{-1}) of HPMC; and the C-C stretch (1500 – 1400 cm^{-1}) as well as the C=O stretch of carbopol which shifted to 1720 -1715 cm^{-1} were maintained in the co-processed polymers while the dimer OH at absorbance range 3400 – 2800 cm^{-1} and the C-H bend at 700 – 600 cm^{-1} showed them as distinct from the parent polymers.

The ranking for the mean projected diameter of the polymer batches was D > F > B > A > E > C >> G. The co-processed polymers did not show a proportional increase in size. The vibrio and rod to needle-like shape of the polymers could have contributed to the irregularity seen in the particle size (Akin-Ajani *et al.*, 2014). Particles with irregular shape cause a decline in the ability of the particles to interlock thus reducing tendencies to pack and break uniformly (Femi-Oyewo *et al*., 2015).

The particle density of the polymers is presented in Table 3. It shows the density of the particles making up the polymer. The particle density ranking of the polymers was of the order F > D > E > A > C > B > G. Carbopol had the highest particle density while HPMC had the least. The co-processed polymers had particle densities that were lower than carbopol but higher than HPMC, indicating that the co-processed particles would have a higher cohesive force than HPMC (Femi-Oyewo *et al*., 2015). An assessment of particle density for materials used in hand sanitizers is important because dense particles may produce dispersions that are more viscous. The viscosity of hand sanitizers adds to their physical outlook and patient acceptability.

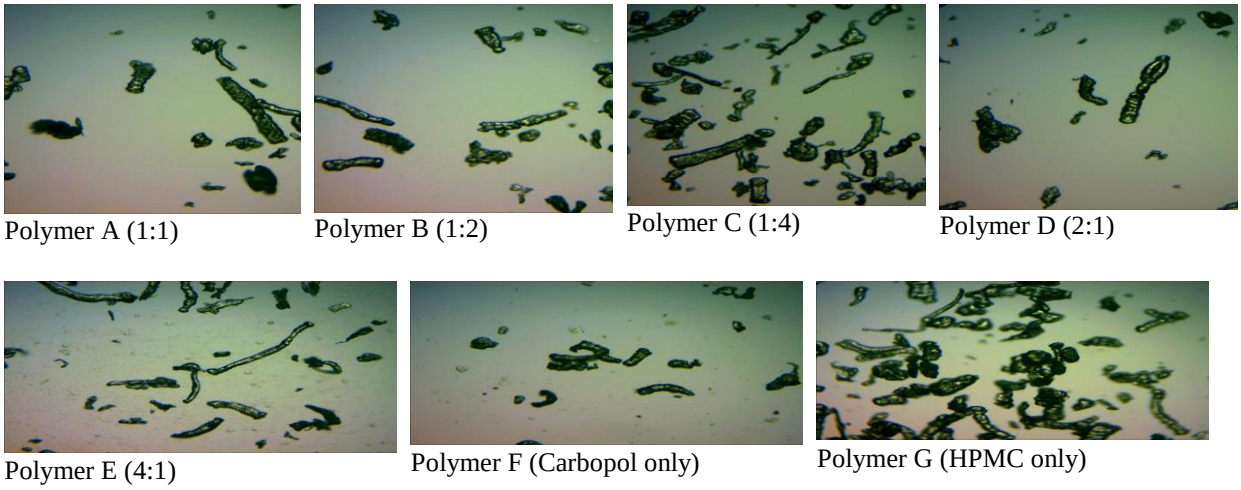

Figure 1. Photomicrographs of the Polymers (x40)

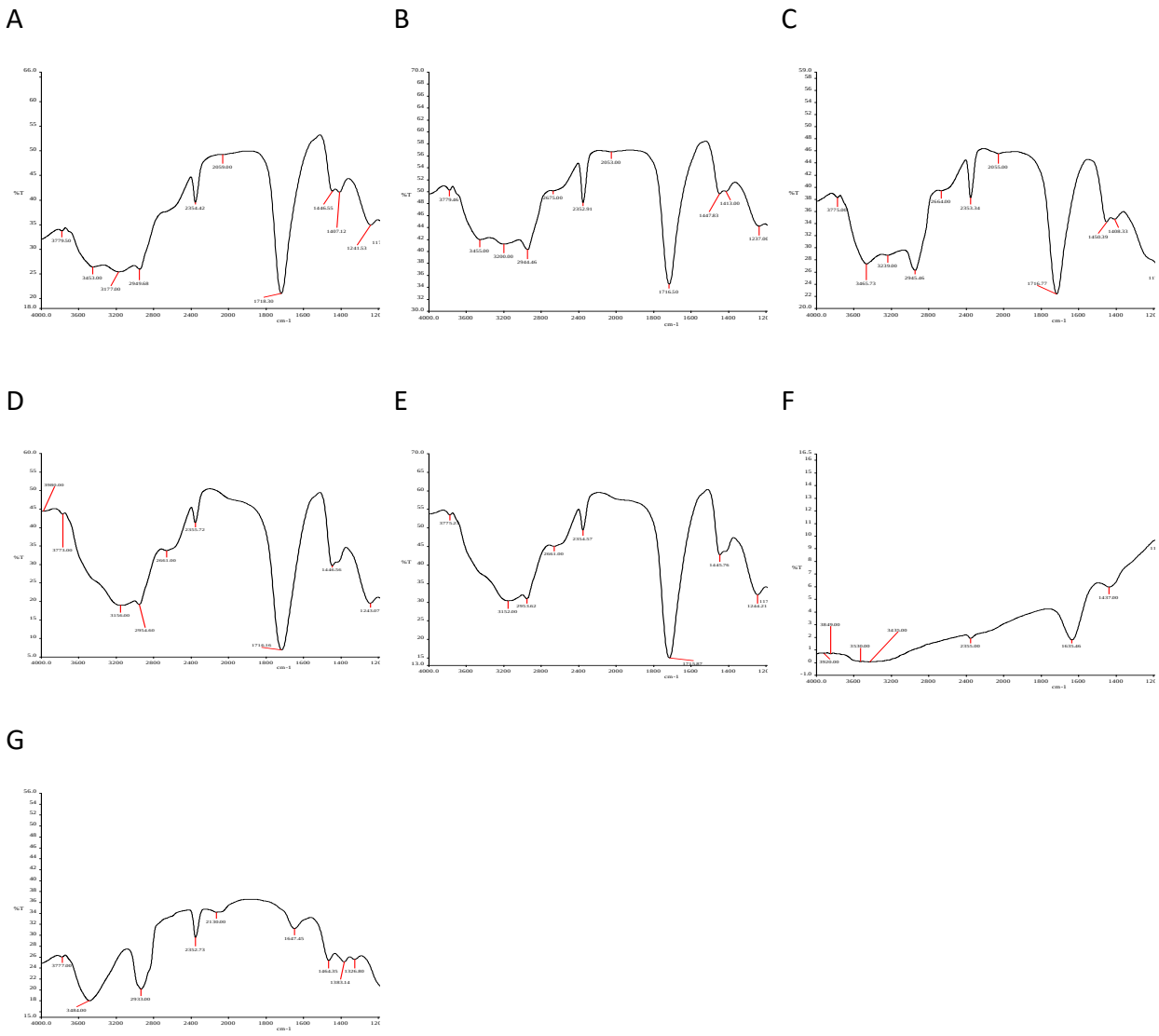

Figure 2. FT-IR spectra of Carbopol (F), HPMC (G) and co-processed forms of both polymers in batches- 1:1(A), 1:2(B), 1:4(C), 2:1(D) and 4:1(E)

The Water Absorption Capacity (WAC) of the polymers is presented in Table 3 and had a rank order of F > E > D > C = A > B >> G. Carbopol had the highest WAC while HPMC had the least. The co-processed polymers with a higher proportion of carbopol had higher WAC than the ones with a higher proportion of HPMC. All of the co-processed polymers had a WAC higher than HPMC alone thus leading to a longer period of hydration and thus higher holding strength of the active ingredient.

Table 3. Material Properties of the Polymers

Polymer Batch	Mean projected Diameter (μm)	Particle Density (gcm^{-3})	Water Absorption Capacity (%)	Hydration Period (h)
A (1:1)	16.41±0.82	1.4464±0.07	280.0±14.0	48
B (1:2)	19.90±0.99	1.3800±0.07	100.0±5.0	48
C (1:4)	12.27±0.61	1.3821±0.07	280.0±14.0	48
D (2:1)	26.74±1.34	1.6602±0.08	500.0±25.0	48
E (4:1)	15.61±0.78	1.6061±0.08	620.0±31.0	72
F (Carbopol)	20.34±1.00	1.7216±0.09	880.0±44.0	336
G (HPMC)	5.45±0.28	1.3606±0.07	20.0±1.0	24

The period of hydration is also presented in Table 3. Hydration period for the polymer batches ranked F >>> E > A = B = C = D > G. This showed the extent of the interaction of the polymers with the water molecules, which also showed the degree at which water is available to the binding sites among the polymers (Akin-Ajani *et al.*, 2014).

The viscosities of the polymer batches measured at 1 and 72 h is presented in Table 4 while the rheological profiles are shown in Figure 3. The co-processed polymers had higher viscosities than HPMC but lower viscosities than carbopol with the ranking A > E > D > B > C. The greater the proportion of HPMC, the lower the value of viscosity obtained. Viscosity also increased with time in all the polymers, suggesting that greater hydration occurred with time. Viscosity generally decreased with increased shear rate. The shear force exerted causes resistance by the fluid to the movement of the spindle, which then determines the viscosity of the fluid. The plot of shear stress against shear rate showed that the polymers had a predominantly pseudoplastic and a non-Newtonian shear thinning behaviour. This has been attributed to the straightening out of the polymer chains during flow and their orientation thus leading to a reduction in viscosity (Crow, 2015). The degree of straightening out and alignment is dependent on the shear rate, with complete disentanglement and full arrangement occurring at sufficiently high shear rates since polymers are tangled and randomly oriented at rest (Crow, 2015).

Table 4. The effect of dispersion time on the viscosity of polymers at 100 rpm

Polymer Batch	Viscosity (cP)	
	1 (h)	72 (h)
A	30.00±1.44	350.00±16.10
B	40.00±1.92	49.00± 2.25
C	27.00±1.30	33.30± 1.53
D	73.00±3.50	116.00± 5.34
E	78.00±3.74	260.00±11.96
F	141.00±6.77	426.00±20.45
G	17.70±0.85	22.00± 1.10

Properties of the Hand Sanitizers

The hand sanitizers were kept in a monitored environment at 25 ± 1 °C with a relative humidity of 56.2 ± 7 %. They were stored in a plastic container with a closure that allowed for easy application of the hand sanitizer. The physical appearance of the hand sanitizers remained the same over the six weeks study period, with a clear light orange colour.

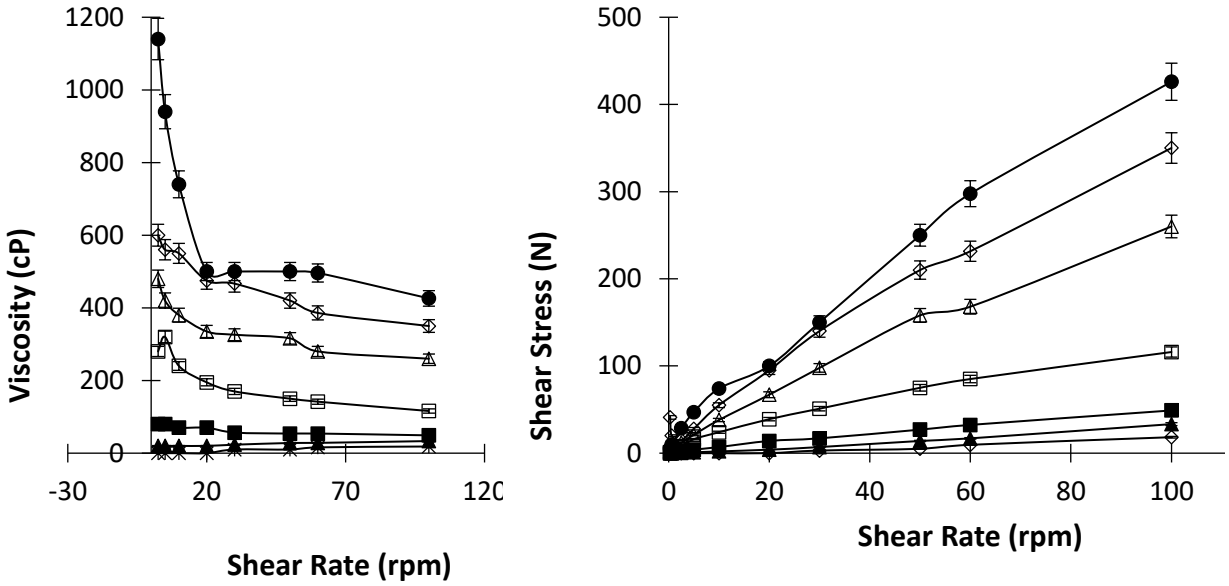

Figure 3. Rheological profiles of the polymers at 72 h

The viscosities for the CAHS and formulated hand sanitizers determined at the first and sixth weeks are presented in Table 5 while the rheology profiles of the hand sanitizers are shown in Figure 4. The results of viscosity for the hand sanitizers prepared using the co-processed polymers were significantly different in comparison with the CAHS. The commercial approved hand sanitizers showed extremely high viscosity values compared to the formulated. These differences are a reflection of the differences in the polymers used. The change in viscosity of the formulated hand sanitizers with time at a constant shear rate of 100 rpm was not significant ($p > 0.05$), though the viscosity of the CAHS decreased with time. The viscosity of the formulated hand sanitizers, however, increased with an increase in shear rate while that of the CAHS decreased with an increase in shear rate. This suggests that the formulated hand sanitizers have a dilatant behaviour while the CAHS exhibited plastic flow. The plots of shear stress against shear rate further confirmed this. The rheogram of the CAHS (Fig. 4b) did not start at the origin which indicated that a yield value existed because of the contacts between adjacent particles (brought about by van der Waals forces), which must be broken down before flow occurs. The mechanism of shear thickening (dilatant behaviour) has been explained thus: at rest, the voids in between the polymers are minimum and the liquid present is sufficient to fill these void spaces. At low, shear rates, the liquid acts as a lubricant thus it eases the motion of each particle past the others and results in stresses that are consequently small. Conversely, at high shear rates, the material expands or dilates such that there is insufficient liquid to fill the increased void space and thus prevent direct contact (solid–solid), which leads to increased friction and higher shear stresses, causing the apparent viscosity to increase rapidly with an increase in the rate of shear (Chhabra and Richardson, 1999, Rapp, 2017).

Table 5. Viscosity, pH, and Transmittance of the Formulated Hand Sanitizers at 0 and 6 Weeks

Formulation Batch	*Viscosity (cP)		pH		% Transmittance	
	0	6	0	6	0	6
A (1:1)	13.30±1.53	13.70±1.15	8.50±0.06	8.50±0.05	74.20±1.21	77.60±0.58
B (1:2)	13.70±0.58	12.30±0.58	8.50±0.23	8.50±0.10	62.10±4.76	78.60±7.16
C (1:4)	13.70±2.08	14.00±1.00	8.00±0.26	8.60±0.08	69.30±4.37	78.90±0.47
D (2:1)	16.00±0.00	15.00±1.00	8.60±0.15	8.80±0.08	67.50±1.12	73.90±0.19
E (4:1)	18.00±0.00	14.00±1.00	8.90±0.10	8.90±0.06	65.80±1.54	73.00±0.53
F (Carbopol)	17.00±2.65	14.30±0.58	8.90±0.00	9.00±0.05	72.80±1.70	79.20±6.93
G (HPMC)	14.70±2.08	15.70±2.08	8.50±0.06	8.30±0.05	73.30±2.73	71.90±3.58
CAHS	3148.00±14.42	3025.00±42.77	6.60±0.25	6.30±0.05	88.20±1.79	82.70±0.79

*Viscosity of formulated hand sanitizers was determined using spindle 03 while that of CAHS was performed using spindle 05 as error readings were obtained at spindle 03.

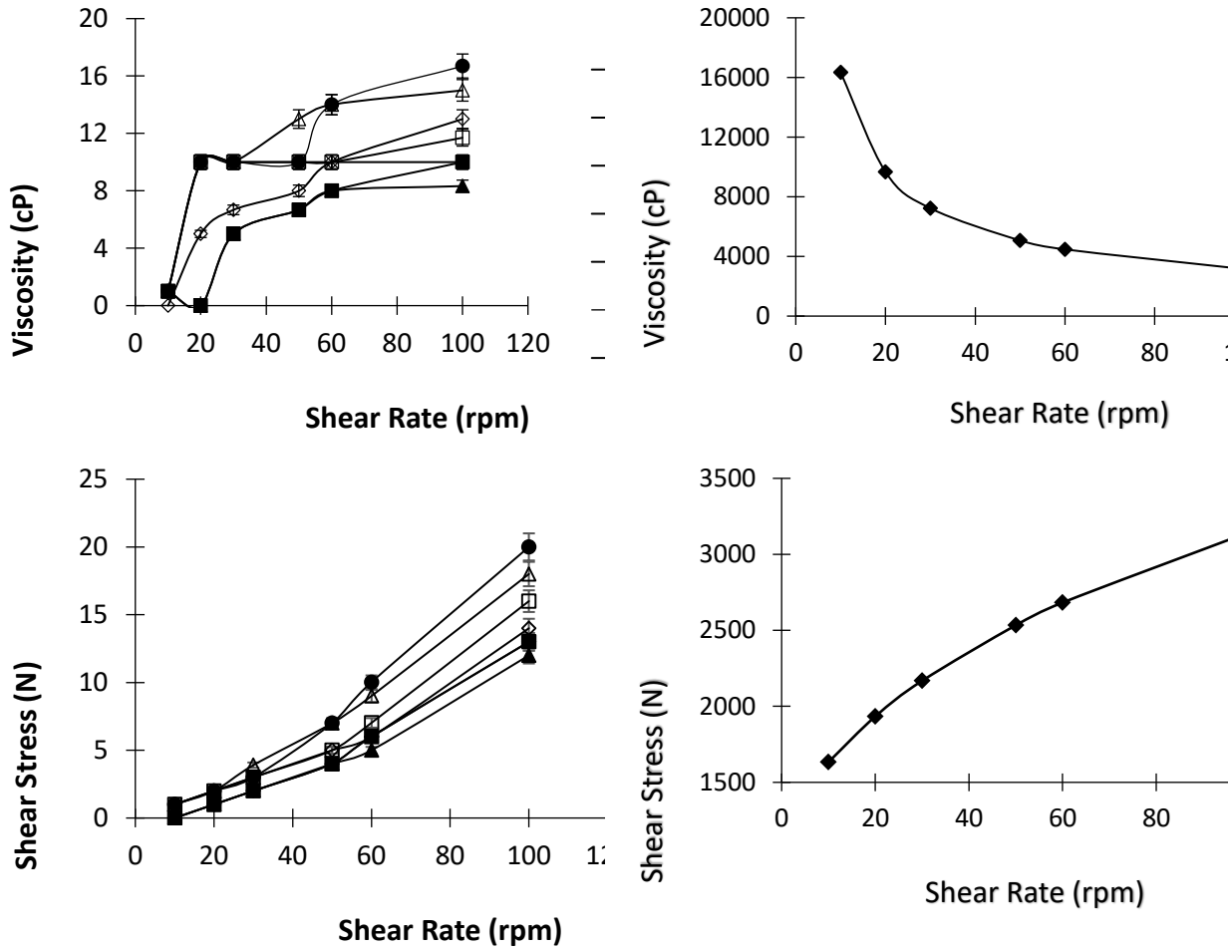

Figure 4. Rheological profile of the formulated hand sanitizers (a) and CAHS (b) at week 1

The pH of the hand sanitizers is presented in Table 5. pH is a measure of the acidity or basicity of a liquid. The formulated hand sanitizers had a basic pH (>7) which was stable over a six week period while that of CAHS ranged between 6.3 – 6.6. The skin has a pH range of 4.2 – 5.6 (Schmid-Wendtner and Korting, 2006). This acidic pH is important in the permeability of substances as well as antimicrobial defence and thus gives the skin its barrier function (Schmid-Wendtner and Korting, 2006). Alteration of these functions can result from using too alkaline formulations. Generally, the skin is remarkably unaffected by alterations in pH, tolerating a range of 3-9 (Isa *et al*., 2000). Furthermore, in a study carried out by Mücke *et al*. (1993) it was found that pH of the hand increased by an average of three units after washing the hands with soap and returned to normal after about 90 min. This indicated, therefore, that an increase in skin pH up to nine would not affect the barrier function of the skin.

The clarity of the hand sanitizers as determined by transmittance is also presented in Table 5. Transmittance is a measure of the amount of light that passes through a transparent material, thus showing the clarity of the liquid or its opacity (Licari and Swanson, 2011). The insignificant difference in the transmittance of the formulated sanitizers and CAHS over time showed that the products did not become cloudy hence a sign of stability.

The rank order of clarity of the hand sanitizers in comparison with isopropyl alcohol (active) was isopropyl alcohol > CAHS > formulated hand sanitizers. Clarity also improved with time, possibly due to improved polymer hydration over time. The reduced clarity in formulated sanitizers may be attributed to the multicomponent nature of the formulations and the manual manufacturing method.

The drying time of the hand sanitizers is presented in Table 6. Although the formulated hand sanitizers displayed a dilatant behaviour, the drying time was still fast. The drying time of the formulated hand sanitizers after application was found to be faster than that of the CAHS, which could be attributed to the high alcohol content of the formulations. The rapid drying of the formulated hand sanitizers did not cause whitening and dryness of the hand nor was there any feeling of stickiness. However, the drying time of the formulated hand sanitizers was longer than that of isopropyl alcohol.

Table 6. Drying Time of the Formulated Hand Sanitizers

Formulation Batch	Drying Time (s)
A	6.8 ± 0.4
B	6.7 ± 0.2
C	7.1 ± 0.2
D	6.9 ± 0.5
E	7.2 ± 0.4
F	7.0 ± 0.3
G	6.7 ± 0.3
CAHS	7.5 ± 0.3
Isopropyl Alcohol	4.6 ± 0.4

The antimicrobial activity of the hand sanitizers was evaluated against some selected microorganisms prevalent in the environment. They all had activities at varying levels against the different microorganisms as shown in Table 7. Only the hand sanitizer containing carbopol: HPMC, 1:1 had no activity against *Candida albicans*. The ranking of the antimicrobial activity of the hand sanitizers was of the order B > F > CAHS > D > E > C > G > A. In comparison, the hand sanitizer prepared with polymer B had the greatest activity. Carbopol with a high WAC probably made penetration of the active agent easier into the agar thus promoting activity against most bacterial organisms evaluated, however, HPMC with poor WAC promoted the activity of the active agent against the fungal isolate. The antimicrobial activity of hand sanitizer prepared with polymer B, compared to the CAHS however, was not significant ($p > 0.05$).

The WHO actually cautions against the use of excipients in alcohol sanitizers because of possible effect on the antimicrobial activity. The antimicrobial results of this study showed that in all cases the formulations demonstrated lower antimicrobial activity compared to the isopropyl alcohol, which is the active agent. A major reason for this may be the flow property of the alcohol, which is Newtonian hence, can easily penetrate the agar matrix and elicit its therapeutic action unlike the formulations, which contain the polymers. The use of polymers as excipients in the delivery of an active ingredient like isopropyl alcohol confers non-Newtonian flow behavior on the formulation being more viscous. While this may pose a slight reduction in the antimicrobial activity, the rheology actually convenes a form of adherence to the molecules of the entire system thus giving it a prolonged action at the site of application. This can be seen also in the significantly higher drying times obtained for the formulations compared to the alcohol. The antimicrobial activity of the formulation was also comparable and higher in

some cases to that of the commercially available hand sanitizer.

The formulation pharmacist is interested in presenting an active ingredient in such a way that it finds acceptability to patients. It is needful for patients to use hand sanitizers as often as necessary for disease prevention. If the product is however not aesthetically pleasing to the patient, its use will be stalled irrespective of notable therapeutic action.

Table 7. Antimicrobial Activity of the Formulated Hand Sanitizers Using the Different Polymers (Mean ± Sd)

Formulation Batch (Carbopol:HPMC)	Zone of Inhibition (mm)				
	S. typhi	***E. coli***	***B. subtilis***	***S. aureus***	***C. albicans***
A (1:1)	14.67±6.43	13.33±2.31	12.67±1.15	12.67±1.15	0.00±0.00
B (1:2)	17.33±2.31	14.67±2.31	16.67±8.08	18.33±5.86	16.00±2.00
C (1:4)	12.00±2.00	14.00±3.46	14.67±3.06	21.00±3.61	12.67±1.15
D (2:1)	15.33±4.16	14.00±4.00	12.67±1.15	16.00±2.00	14.67±4.16
E (4:1)	14.67±5.03	14.67±1.15	12.00±2.00	14.00±0.00	14.67±1.15
F (Carbopol)	17.33±4.16	16.00±2.00	18.00±2.00	16.00±3.46	16.00±2.00
G (HPMC)	13.33±2.31	13.33±2.31	13.33±1.15	15.33±4.16	18.00±0.00
CAHS	16.67±3.06	18.00±2.83	13.00±1.41	13.00±1.41	14.00±2.83
Isopropyl alcohol	23.00±4.36	24.33±4.04	24.50±0.71	20.67±1.15	15.00±1.41

KEY: S. typhi=Salmonella typhi; E. coli= Escherichia coli; B. subtilis= Bacillus subtilis; S. aureus= Staphylococcus aureus; C. albicans= Candida albicans

This study is novel because co-processing of excipients has been mostly applied to solid formulations. The study successfully co-processed carbopol and HPMC to obtain newer excipients, which could find application in the preparation of hand sanitizers or other liquid dosage forms. The successful usage of the co-processed excipient in a liquid formulation is a worthwhile venture. The study has thus expanded the usefulness of these polymers to serve as raw materials for newer excipients with multifunctional properties.

CONCLUSION

Co-processing of carbopol with HPMC led to a reduction in hydration time of carbopol resulting in faster formulation time. Co-processing of the excipients improved the pharmaceutical properties of the hand sanitizers. Though the antimicrobial activity of the formulated hand sanitizers corroborated the concerns raised by WHO, the longer drying times would confer prolonged activity at the site of application. The hand sanitizer formulation prepared with polymer blend, B, carbopol: HPMC of ratio 1:2 demonstrated optimum antimicrobial and pharmaceutical properties and could be further developed for commercial use in this regard.

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*Address for correspondence: Olufunke D. Akin-Ajani
Department of Pharmaceutics & Industrial Pharmacy,
University of Ibadan,
Ibadan, Nigeria
Telephone: +234 8023007412
E-mails: oakinajani@yahoo.com

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