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^{26}Al -containing acidic and basic sodium aluminum phosphate preparation and use in studies of oral aluminum bioavailability from foods utilizing ^{26}Al as an aluminum tracer

Robert A. Yokel^{a,b,*}, Aaron A. Urbas^c, Robert A. Lodder^{a,c},
John P. Selegue^c, Rebecca L. Florence^a

^a College of Pharmacy, 511C Pharmacy Building 725 Rose Street, University of Kentucky Medical Center, Lexington, KY 40536-0082, USA

^b Graduate Center for Toxicology, University of Kentucky, Lexington, KY 40536-0305, USA

^c Department of Chemistry, University of Kentucky, Lexington, KY 40506-0055, USA

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Abstract

We synthesized ^{26}Al -containing acidic and basic (alkaline) sodium aluminum phosphates (SALPs) which are FDA-approved leavening and emulsifying agents, respectively, and used them to determine the oral bioavailability of aluminum incorporated in selected foods. We selected applicable methods from published syntheses (patents) and scaled them down (~3000- and 850-fold) to prepare ~300–400 mg of each SALP. The ^{26}Al was incorporated at the beginning of the syntheses to maximize ^{26}Al and ^{27}Al equilibration and incorporate the ^{26}Al in the naturally-occurring Al-containing chemical species of the products. Near infrared spectroscopy (NIR) and X-ray powder diffraction (XRD) were used to characterize the two SALP samples and some intermediate samples. Multi-elemental analysis (MEA) was used to determine Na, Al and P content. Commercial products were included for comparison. Satisfactory XRD analyses, near infrared spectra and MEA results confirmed that we synthesized acidic and basic SALP, as well as some of the syntheses intermediates. The ^{26}Al -containing acidic and basic SALPs were incorporated into a biscuit material and a processed cheese, respectively. These were used in oral bioavailability studies conducted in rats in which the ^{26}Al present in blood after its oral absorption was quantified by accelerator mass spectrometry. The results showed oral Al bioavailability from acidic SALP in biscuit was ~0.02% and from basic SALP in cheese ~0.05%, lower than our previous determination of Al bioavailability from drinking water, ~0.3%. Both food and water can appreciably contribute to the Al absorbed from typical human Al intake.

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* Corresponding author. Tel.: +1 859 257 4855; fax: +1 859 323 6886.
E-mail address: ryokel@email.uky.edu (R.A. Yokel).

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Acidic SALP, $\text{NaAl}_3\text{H}_{14}(\text{PO}_4)_8 \cdot 4\text{H}_2\text{O}$ [10305-76-7], is used in the food industry as a leavening agent in baked goods, for example Levair[®], BL-60[®] and actif 8[®]. Basic SALP, $\text{Na}_8\text{Al}_2\text{OH}_2(\text{PO}_4)_4$ [39422-25-8], is used as an emulsifying agent in processed cheese. The Na–Al–P ratio in acidic SALP is 1:3:8 and in basic SALP is 8:2:4. They are quite water-insoluble but are soluble in dilute hydrochloric acid [1,2]. For example, we found that 50 mg acidic SALP dissolved in 840 μl of concentrated HCl. Their loss on ignition at 750–800 °C after 2 h is 19.5–21% and not more than 9%, respectively [1,2]. Basic SALP is reported to be quite hygroscopic. It is commercially available as Kasal[®], which contains $\sim 30\%$ dibasic sodium phosphate. Acidic SALP appeared to also be quite hygroscopic.

The objective was to synthesize ^{26}Al -containing acidic and basic SALPs for use in studies to determine the oral bioavailability of aluminum incorporated in selected foods. The ^{26}Al was incorporated at the beginning of the synthetic scheme to maximize the likelihood that it would equilibrate with the ^{27}Al present and would exist in the same chemical form (species) as the aluminum normally present in SALPs. The samples, and some of the intermediates in their syntheses, were validated by several analytical measures.

Acidic SALP was prepared to contain ~ 1 nCi (50 ng) ^{26}Al /10 mg SALP by addition of ^{26}Al (obtained from the Purdue Rare Isotope Measurement [PRIME] Lab) that had a $^{26}\text{Al}/^{27}\text{Al}$ ratio of 1:35. As the ^{26}Al represented 0.2% of the total Al in the acidic SALP, additional ^{27}Al , from $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$ (Fisher Scientific), was incorporated into the synthesis.

To synthesize ^{26}Al -containing acidic SALP an appropriate method was selected from among the published syntheses, which appeared to be amenable to scaling down to prepare ~ 300 – 400 mg of the sample. Published synthetic methods for acidic

SALP include a patent that describes condensation of water vapor during monitoring of the viscosity of the reaction mixture [3]. The sample was identified by XRD, but the pattern was not described. Other patents described acidic SALP production by spray drying [4], utilizing a fluidized bed [5] and utilizing a heated kneading apparatus [6]. The equipment necessary for these procedures was not available to us and we realized that these methods would not readily lend themselves to small-scale production. Therefore, we chose an earlier method that did not require special equipment [7]. The described procedure entailed addition of 108 g of Na_2CO_3 to 3376 g of 75% H_3PO_4 at 70 °C, heating to 90 °C and slow addition of 458 g of $\text{Al}(\text{OH})_3$. The solution was heated with stirring and boiled down, with stirring, until the boiling point reached 135 °C. At this point, when we conducted the synthesis scaled down 3000-fold, we observed the appearance of solid material. As described in the patent, the sample was cooled to room temperature, two volumes of 75:25 MeOH:H₂O were added and the suspension was filtered. The crystals were washed with MeOH:H₂O and then MeOH to remove free H_3PO_4 , and dried at 70 °C. We scaled the method down to $\sim 1/3000$ of the above and conducted the reaction to produce acidic SALP ~ 53 times, while modifying the reaction to optimize the sample. We initially followed the method, scaled down, incorporating the Al as described, then as AlCl_3 in solution and as a solid, and finally as $\text{Al}(\text{OH})_3$ dissolved in the H_3PO_4 . Most samples were characterized by using XRD and NIR. The ~ 15 last SALP samples were also characterized by using inductively coupled plasma spectrometry to conduct MEA of Na, Al and P. Many of the syntheses were conducted to assess the influence of the number of washes and the ratio and volume of the MeOH:H₂O to maximize yield and sample quality. One wash of 3 ml of 75:25 MeOH:H₂O, two

washes of 3 ml 90:10 MeOH:H₂O and then a wash of 3 ml MeOH were found to be best. The ²⁶Al was incorporated into the acidic SALP reaction mixture as ²⁶Al(OH)₃, prepared by its precipitation from an aqueous solution of ²⁶Al and ²⁷Al-Cl₃·6H₂O by addition of NaOH to pH 6.2, the nadir of Al solubility in the absence of solubilizing ligands [8]. Because we were unable to completely dry the Al(OH)₃, we used it as a slurry. This also helped to overcome the difficulty of quantitatively transferring the Al(OH)₃ and dispersing powdered Al(OH)₃ in the reaction mixture. The Al(OH)₃ slurry was washed twice with 2 ml of water, followed by centrifugation and characterized by NIR in the 10-ml glass round-bottomed flask in which it was generated. More than two washes produced unacceptable aluminum loss in the washes. The flasks would not tolerate high speed centrifugation. Total aluminum was determined by electrothermal atomic absorption analysis (ETAAS) by using a Perkin–Elmer 4100 ZL atomic absorption spectrophotometer. The samples were monitored by NIR of the Al(OH)₃ slurry in the glass flask. The Al(OH)₃ slurry was added directly to the acidic SALP reaction mixture.

NIR and XRD were chosen to characterize the Al(OH)₃ slurry and the acidic SALPs because they are non-destructive methods. We wanted minimal ²⁶Al-SALP loss due to the high cost of the ²⁶Al (\$100/nCi) and the effort invested in ²⁶Al-SALP synthesis and validation. NIR spectra were obtained from three readings of the sample, obtained at 120° rotations in the sample holder. A Bran+Luebbe InfraAlyzer 500 was used, scanning from 1100 to 2500 nm. The Al(OH)₃ slurry and dry SALPs were contained in glass tubes. The results were compared to the NIR spectra obtained from a freshly prepared slurry of commercial Al(OH)₃ (aluminum hydroxide hydrate, Sigma Chemical Co.) or a commercial acidic SALP (Spectrum Labs). We found only one published report of a NIR spectrum of Al(OH)₃ [9]. However, this report describes a dry material. We found no published reports of NIR spectrometry of acidic SALP. Fig. 1 shows the NIR spectra of the ²⁶Al-containing Al(OH)₃ slurry that was used in the production of the ²⁶Al-containing acidic SALP and a slurry prepared from commercial Al(OH)₃.

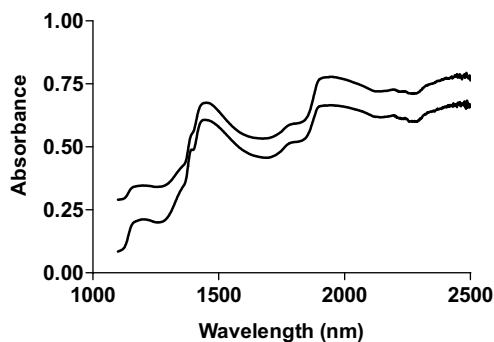


Fig. 1. Near infrared (NIR) spectra of aluminum hydroxide. Upper spectrum: a slurry prepared from commercial Al(OH)₃ (to which 0.1 absorbance unit was added to each value to offset it from the lower spectrum). Lower spectrum: the ²⁶Al-containing Al(OH)₃ slurry that was used in the production of the ²⁶Al-containing acidic SALP.

A principal component analysis (PCA) was performed on the entire collection of NIR spectra obtained from the acidic SALPs we synthesized and commercial products used as references. PCA was used to reduce data dimensionality and facilitate the comparison of our synthetic samples and the commercial reference samples [10,11]. The primary, secondary and tertiary components were determined to be significant, and accounted for 63%, 24% and 7% of the total variance in the data set. Graphs of the primary versus secondary and secondary versus tertiary components of the commercial product and all of the acidic SALPs we prepared showed the deviation of each of our samples from the commercial product. These results were used to evaluate our modifications of the synthesis to guide development of the procedure to prepare an acidic SALP. Fig. 2 shows the primary versus secondary components of the variance of the acidic SALPs. Another analysis of the variance excluding the contribution from the peaks attributed to water (1400 to 1500 nm and 1900 to 2050 nm) showed comparable results, suggesting that water was not the major contributor to the differences among our samples and the commercial acidic SALP. The overall variance between each of our acidic SALPs and the commercial product was calculated by using the Bootstrap Error-Adjusted Single Sample Technique (BEAST) method [12] which allows one to make

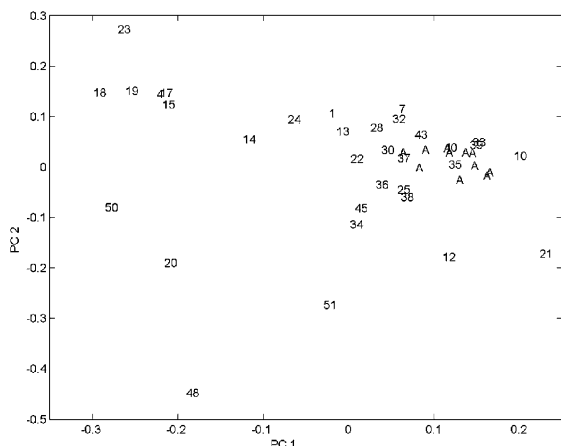


Fig. 2. The variance of acidic SALP NIR spectra compared to the commercial product, graphed as the primary (PC 1) versus the secondary (PC 2) components of the variance. Numbers note our acidic SALP products. “A” notes the commercial product. Greater vertical distance from A notes greater difference between our samples and the commercial product for the principal component of variance. Greater horizontal difference between our sample and the commercial product notes a greater difference for the secondary component of variance.

an estimate of the multidimensional standard deviation from the commercial product. In this technique, the non-averaged (raw) NIR spectra obtained from the three determinations of each of 11 samples of the commercial acidic SALP were collected as a target (reference spectra). Then a BEAST standard deviation from this population was found. These standard deviations were corrected for the number of training samples and the number of wavelengths. The average number of standard deviations for each of the samples from the reference was determined. Three standard deviations is a reasonable cutoff for exclusion from the training population. The mean BEAST standard deviation for 37 acidic SALP samples was 7.37 (SD = 5.47), with a range of 1.56–24.86.

The NIR spectra of the ^{26}Al -containing acidic SALP and the commercial acidic SALP are shown in Fig. 3. Water significantly contributed to the absorbance at 1450 and 1950 nm. When we heated one of our aluminum-containing acidic SALPs and the commercial product to 215 °C for 2 h, we observed loss of most of the absorbance at these wavelengths.

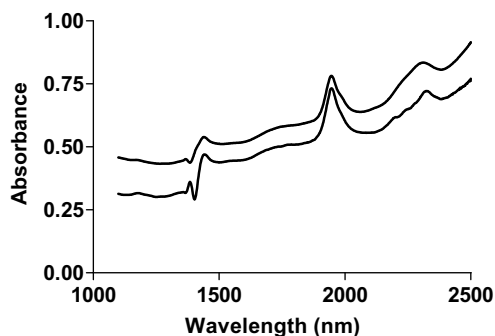


Fig. 3. Near infrared (NIR) spectra of acidic SALP. Upper spectrum: a commercial acidic SALP (offset by 0.1 absorbance unit). Lower spectrum: the ^{26}Al -containing acidic SALP.

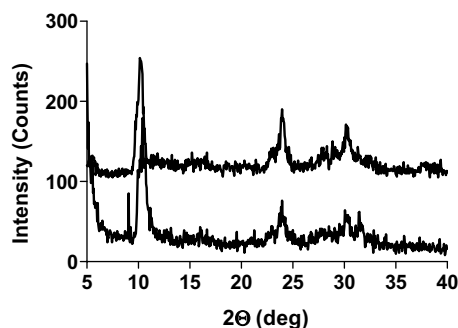


Fig. 4. Powder XRD pattern of acidic SALP. Upper spectrum: a commercial acidic SALP (offset by 100 counts). Lower spectrum: the ^{26}Al -containing acidic SALP.

To obtain XRD of acidic SALPs, a Rigaku Geiger flex X-ray diffractometer was used. Each diffraction pattern was obtained from 5° to 85° on 2θ with a step size of 0.05° at a rate of 6.0°/min. Fig. 4 shows the part of the XRD pattern of the ^{26}Al -containing acidic SALP and a commercial acidic SALP that had characteristic peaks. Finding no published XRD data for acidic SALP, we compared our sample to the commercial product. The peaks of the commercial product and our sample were seen at 10.5°, 24.1° and 30.2° on 2θ , suggesting similar composition. Heating one of our acidic SALP samples and the commercial product to 225 °C for 2 h resulted in peaks at 11.7°, 23.3° and 26.6° for both samples. The peak in our sample at $\sim 31^\circ$ on 2θ , which was not seen in the commercial product, did not disappear when the sample was heated to 215 °C for 2 h, suggesting that it

was not due to water. It was thought to be due to $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$ because there was some residual chloride in the $\text{Al}(\text{OH})_3$ after the second wash.

We also characterized several of our acidic SALP samples for Na, Al and P content using MEA. The results were used to guide the amounts of Na_2CO_3 , H_3PO_4 and $\text{Al}(\text{OH})_3$ added. Solutions of our acidic SALP samples and the commercial acidic SALP were prepared in 0.1 N HCl and compared to standards containing 3.2, 12.6, 25.3, 50.6 and 101.2 ppm Na; 6.2, 12.5, 24.9 and 49.8 ppm Al; and 6.3, 12.6, 25.3, 50.6 and 101.2 ppm P, similarly prepared from commercial atomic absorption standards (Aldrich Chemical Co.). Solutions were analyzed by using a Spectro Analytical inductively-coupled plasma spectrophotometer with the torch set at a radial orientation. MEA of the ^{26}Al -containing acidic SALP showed Na, Al and P content to be 102%, 100% and 91% of theoretical. Sample yield was 309 mg, 50% of theoretical.

Thermogravimetric analysis was conducted to ascertain mass loss on heating acidic SALP samples. The instrument was a Hi-Res TGA 2950 thermogravimetric analyzer, controlled by Thermal Advantage Control software using TA Universal Analysis graphics software. Nitrogen was the inert gas. Mass loss was primarily seen from 80 to 200 °C and 200 to 300 °C. No mass was lost from 700 to 900 °C. Mass loss of one of our samples that had been dried at 80 °C, when heated from 90 to ~200 °C, was ~7.5% of the mass, based on a M_r of 949 for acidic SALP ($\text{NaAl}_3\text{H}_{14}(\text{PO}_4)_8 \cdot 4\text{H}_2\text{O}$). The four waters of hydration, which have a mass of 7.59%, could have provided this loss. Very similar mass was lost when our samples ($18.8 \pm 1.3\%$, $n = 8$) and the commercial product (18.8%, $n = 2$) were heated to 500 °C, consistent with expected loss on ignition of 19–21% for acidic SALP [2].

In summary, NIR spectra of the ^{26}Al -containing $\text{Al}(\text{OH})_3$ used to prepare the ^{26}Al -containing acidic SALP as well as the acidic SALP were quite similar to the commercial products (Figs. 1 and 2). The XRD patterns of the ^{26}Al -containing acidic SALP had peaks at the same 2θ values as the commercial product (Fig. 3). Mass loss on heating non- ^{26}Al -containing acidic SALP samples and a commercial product were quite similar and consistent with expected values for this material. Analyses of the

Na, Al and P content of the ^{26}Al -containing acidic SALP were acceptable. These results confirmed production of a ^{26}Al -containing acidic SALP.

A commercial acidic SALP was used to dilute some of the ^{26}Al -containing SALP to result in ~1 nCi $^{26}\text{Al}/20$ mg acidic SALP as well. These two acidic SALP samples were incorporated into a biscuit material, to final acidic SALP concentrations of 10 and 20 mg/g (1% and 2%) biscuit. Approximately 1 g of each of the biscuit materials was eaten by five rats from which blood was drawn before and repeatedly after biscuit consumption. Analysis of blood serum samples for ^{26}Al by accelerator mass spectrometry (AMS) (Fig. 5) enabled determination of the area under the ^{26}Al -serum-concentration curve (AUC) from which the oral bioavailability of aluminum was determined. The percentage of Al absorbed from biscuit material averaged ~0.02%.

Basic SALP was prepared to contain ~1 nCi (50 ng) $^{26}\text{Al}/15$ mg by addition of the ^{26}Al from the PRIME Lab described above. As the ^{26}Al represented 0.15% of the total Al in the sample, additional ^{27}Al was added, as above.

One of the published synthetic methods for basic SALP is a patent that entails combining the reactants and evaporating the solvents to produce basic SALP by total evaporation [13]. We modified this method, in which 162 g anhydrous Na_2HPO_4 is dissolved in 72 g 85% H_3PO_4 in 450 ml of distilled water. The solution was heated to ~80 °C and 102 g of sodium aluminate was added slowly with good agitation. The resultant slurry was dried

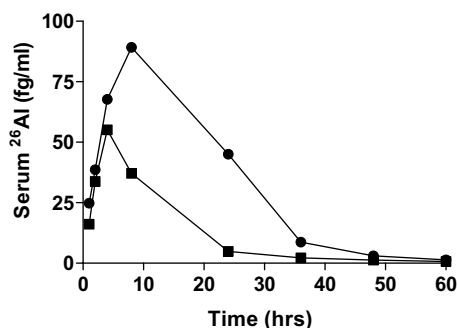


Fig. 5. Serum ^{26}Al concentration versus time after oral consumption of ^{26}Al in biscuit or cheese. Results are means. Squares are results from biscuit, circles from cheese.

by pouring it onto a stainless steel surface that was preheated to $\sim 150^\circ\text{C}$. We modified the method to $\sim 1/850$ scale and prepared ~ 28 samples. To incorporate the ^{26}Al into basic SALP we prepared ^{26}Al -containing sodium aluminate. Initially $\text{Al}(\text{OH})_3$ was prepared by adding NaOH to an aqueous solution of Al (introduced as $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$) to an r value of 3. The r value is the number of moles of OH^- added per mole of Al . The sample was centrifuged at $\sim 15,000g$ force in Oakridge polysulfone centrifuge tubes and washed six times, with centrifugation, with 2 ml of Milli-Q[®]-prepared water to remove sodium and chloride ions. Chloride in the washes was semi-quantified by using the silver nitrate method (e.g. #46.5.02 in [14]) by visually comparing the precipitate formed to that produced by known chloride concentrations. The last wash had $\sim 200\text{--}300$ ppm Cl , representing $<1\%$ of the chloride introduced from the $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$, indicating very little chloride remained after the six washes. The aluminum lost in the washes was quantified by ETAAS analysis. The total loss of the added aluminum in the six washes was $\sim 1\%$. The $\text{Al}(\text{OH})_3$ was converted to sodium aluminate by addition of NaOH to an r value of 5.5 [15], which was selected to provide an 8:2:4 Na:Al:P ratio when combined with the other reactants. We were unable to obtain by lyophilization a dry sodium aluminate sample, so worked with this intermediate as synthesized, a viscous, cloudy liquid.

The sodium aluminate was not amenable to good characterization by NIR or XRD. Some sodium aluminate samples we prepared were subjected to drying for several weeks and compared to a commercial (Sigma) sodium aluminate by using MEA conducted with a Thermo Jarrell Ash IRIS Advantage Dual View ICP. Interpretation of the results is influenced by the sodium aluminate formula used. Two common examples, of the many described sodium aluminates, are NaAlO_2 ; [11138-49-1] and $\text{NaAl}(\text{OH})_4$; [12251-53-5]. Therefore, the amount of aluminum and sodium added to form the sodium aluminate was guided by MEA of the basic SALP, rather than the sodium aluminate.

The final samples of sodium aluminate were prepared from 300.9 mg $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$ plus 0.747 ml of 5 M NaOH to make 3.73 mmol

$\text{Al}(\text{OH})_3$, to which 0.622 ml of 5 M NaOH was added to make sodium aluminate. To make the basic SALP, 132.6 mg Na_2HPO_4 in 200 mg water and 180 mg 85% H_3PO_4 were slowly added to the sodium aluminate. This milky suspension was poured onto a stainless steel surface at 80°C to avoid the splattering experienced when the surface was at 150°C . The temperature was increased to 100°C for 15 min, then to 150°C for 2 h. The basic SALP was scraped off and dried at 100°C for 12 h as described [13].

The sodium aluminate solution had no NIR characteristics that could be used to characterize it. It was characterized by using Raman spectroscopy, measured on a Digilab FTS 4000 with a FT-Raman accessory. A liquid nitrogen-cooled Ge detector was used with a NdYAG laser emitting 512 mW at 1064 nm. Each spectrum was scanned 259 times at a resolution of 8 cm^{-1} . Solutions containing several concentrations of our samples were compared to solutions of similar concentrations of commercial sodium aluminates (Sigma, Pfaltz and Bauer) in water. The spectrum in the $500\text{--}750\text{ cm}^{-1}$ region was used, as described [16]. All of the spectra were very similar for the band at $\sim 618\text{ cm}^{-1}$, with the exception of one of the Sigma sample dilutions, which had the band center shifted to 612 cm^{-1} . Correlation analysis of the spectra, calculated as described [17], comparing the spectral match indices between all possible pairings of the Raman spectra, showed our sample (prepared at 0.14, 0.35 and 0.69 M) most closely resembled the Sigma (0.21 M), Pfaltz and Bauer (0.20 M) and Pfaltz and Bauer (0.51 M) solutions, respectively. The results suggest that we successfully prepared sodium aluminate (personal communication, Dr. Chris Brown).

The basic SALP samples were characterized by NIR as described above, XRD (using a Siemens Diffraktometer D500 with Kristalloflex data processing) and MEA. We found no published NIR spectra of basic SALP. We were unable to identify a commercial source of pure basic SALP; therefore, we determined the NIR spectra attributable to basic SALP from the NIR of Kasal[®], which contains $\sim 30\%$ dibasic sodium phosphate, compared to the spectra from commercial dibasic sodium phosphate (Fisher Scientific). The spectra of dibasic

sodium phosphate had few significant NIR features. Addition of dibasic sodium phosphate to Kasal[®], to generate total dibasic sodium phosphate percentages of 30% to 65%, did not change the NIR spectrum. Therefore, dibasic sodium phosphate was not considered to significantly contribute to the Kasal[®] NIR spectrum. In contrast to the peak attributed to water at 1450 nm in acidic SALP, the peak at 1420 nm in basic SALP was not attributed to water because it did not decrease after drying a Kasal[®] sample at 120 °C for 12 h. Absorbance at 1420 nm is most likely due to the OH groups in basic SALP. However, the presence of water, which increased hydration of Kasal[®], did increase NIR absorbance in a broad peak between 1890 and 2100 nm. Fig. 6 shows the NIR spectra of the two final basic SALP samples and Kasal[®]. The results are consistent with successful synthesis of ²⁶Al-containing basic SALP.

The XRD pattern of basic SALP has been described as having principal lines at ~ 4.77 , 3.57, 2.63, 2.56 and 2.51 Å [13], equivalent to 2θ values of 15.59°, 24.92°, 34.06°, 35.02° and 35.74°. We compared our samples to Kasal[®], which contains $\sim 30\%$ sodium phosphate dibasic, and to sodium phosphate dibasic. Sodium phosphate dibasic produced some peaks that appear to correspond to peaks in the Kasal[®] spectra but are less pronounced in the spectra of our samples. The results are shown in Fig. 7. They suggest that we successfully prepared ²⁶Al-containing basic SALP.

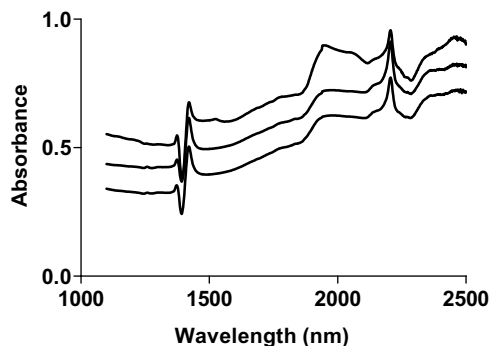


Fig. 6. NIR spectra of basic SALP. Upper spectrum: A commercial basic SALP (Kasal[®]) (offset by 0.2 absorbance unit). Middle spectrum: the non-²⁶Al-containing basic SALP (to which 0.1 absorbance unit was added to each value). Lower spectrum: the ²⁶Al-containing basic SALP.

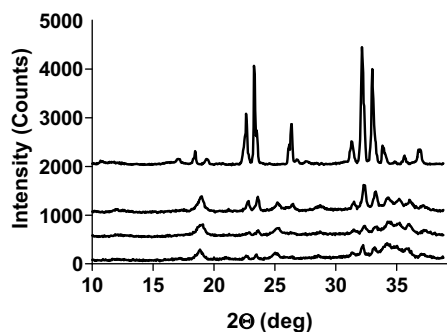


Fig. 7. Powder XRD pattern of sodium phosphate dibasic and basic SALPs. Top spectrum: a commercial sodium phosphate dibasic (offset by 2000 counts). Second from top spectrum: Kasal[®] (offset by 1000 counts). Third spectrum: the non-²⁶Al-containing basic SALP (offset by 500 counts). Lowest spectrum: the ²⁶Al-containing basic SALP, prepared concurrently with the non-²⁶Al-containing basic SALP.

Analysis of the Na, Al and P content of the ²⁶Al-containing basic SALP showed 95%, 97% and 96%, respectively, of theoretical composition for basic SALP; Na₈Al₂OH₂(PO₄)₄. Product yield was 396.3 mg, 98% of theoretical. A concurrently prepared non-²⁶Al-containing basic SALP had Na, Al and P contents of 94%, 90% and 98% of calculated values, with a yield of 101% of theoretical.

In summary, the Raman spectroscopy patterns, characterized by a peak at 618 cm⁻¹, of our sodium aluminate samples were very similar to those of a commercial product. The NIR and XRD spectra of the ²⁶Al-containing basic SALP and a commercial product (Kasal[®]), containing $\sim 70\%$ basic SALP and 30% sodium phosphate dibasic, were quite similar (Figs. 6 and 7), particularly when one considers the contribution of sodium phosphate dibasic to the Kasal[®] XRD spectra. Analysis of the Na, Al and P content of the ²⁶Al-containing basic SALP was acceptable. These results confirmed successful production of a ²⁶Al-containing basic SALP.

When the ²⁶Al-containing basic SALP was prepared, non-²⁶Al-containing basic SALP was concurrently and identically prepared, which was used to dilute some of the ²⁶Al-containing sample to result in ~ 1 nCi ²⁶Al/30 mg basic SALP as well. These two basic SALP samples were added to a final basic SALP concentration of 15 and 30 mg/g

(1.5% and 3%) processed cheese. Approximately 1 g of each of the cheese materials was eaten by six rats from which blood was drawn before and repeatedly after cheese consumption (Fig. 6) to enable determination of percentage of Al absorbed from cheese using the same method as for biscuit, above. Oral Al bioavailability from cheese averaged $\sim 0.05\%$.

We previously used the same methods to determine oral Al bioavailability from drinking water, using ^{26}Al as a tracer with AMS quantification. The percentage of Al absorbed was $\sim 0.3\%$ [18]. Given that humans consume an average of 100 and 7500 mcg Al daily in drinking water and food, respectively [19], and that the present results show Al absorption from water is ~ 10 -fold greater than from food, the contribution of absorbed Al from food is ~ 10 -fold greater than from water. However, food and water Al concentrations vary considerably which would influence the relative contributions of these two sources to absorbed aluminum.

Acknowledgments

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