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Research Article

Tissue Kinetics of Medicinal Synthetic Aluminum Magnesium Silicate in Broilers Chicks

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Abstract

Medicinal synthetic aluminum magnesium silicate (MSAMS), a naturally derived nanomaterial, is produced via controlled synthesis from two pharmacopeially recognized silicates: aluminum silicate and magnesium silicate with dextrose monohydrate as a carrier. The parent product, Aluminum magnesium silicate (AMS) is generally regarded as non-absorbable from the gastrointestinal tract and is believed to exert its effects locally but contrary to this facts, AMS in the form of MSAMS can become absorbable from the gastrointestinal tract into systemic circulations. To verify this, 38 six-week old broiler-chicks were drenched with a single dose of MSAMS at 50 mg/kg and two birds were sacrificed post treatment at 120 hours, 240 hours, 360 hours and 480 hours for their livers, brains, kidneys, hearts and skeletal muscles used for tissue-MSAMS concentrations. Means of MSAMS concentrations in brains of broilers at 120, 240, 360 and 480 hours PT (0.72 ± 0.10, 0.52 ± 0.05, 1.39 ± 0.11 & 0.24 ± 0.02) were significantly lower (p > 005) compared to mean concentrations of msams in liver (2.41 ± 0.23, 2.51 ± 0.36, 2.18 ± 0.07 & 2.10 ± 0.20) and muscle tissues (2.41 ± 0.13, 1.14 ± 0.06 1.26 ± 0.06 & 3.04 ± 0.14) at different time interval. The elimination half-lives of MSAMS in the brain (0.026 ± 0.003), liver (1.03 ± 0.28) and muscle (0.21 ± 0.04) were significantly different (p > 0.05) from that in the heart and kidney where their elimination half-lives were not applicable because of negative elimination rate constant, indicating that msams concentration increases over the terminal phase (360-480 hours) in these tissues thus reflecting ongoing tissue uptake or redistribution rather than elimination.

Keywords: MSAMS; Tissues Kinetics; Broilers

Introduction

Aluminum magnesium silicate (AMS) is a complex compound and natural ore which occurs as mineral deposits, (USP, 2020). It is widely used in pharmaceutical formulations as an adsorbent, stabilizing agent, and suspending agent [1]. Medicinal Synthetic Aluminum Magnesium Silicate (MSAMS) is a formulation composed of aluminum magnesium silicate (AMS), an approved medicine [1] and dextrose monohydrate (a simple sugar). The sugar component facilitates the transport of AMS nanoparticles across mucous membranes [2]. Both AMS and aluminum silicate and magnesium silicate that are used in synthesizing Medicinal synthetic aluminum magnesium silicate (MSAMS) are independently listed as approved medicines in major international pharmacopeia. They are recognized as pharmaceutical-grade excipients with antacid, antiulcer and antidiarrheal properties [1,3,4]. The controlled synthetic route employed in the production of MSAMS ensures that the resulting aluminum magnesium silicate product is free of the mineral contaminants found in naturally mined smectite

clays, thereby meeting pharmaceutical-grade purity standards required for biomedical application [5]. [6] synthesized AMS from two medicinal minerals, Aluminum silicate ($Al_4(SiO_4)_3$) and Magnesium silicate (Mg_2SiO_4). Aluminum silicate ($Al_4(SiO_4)_3$) and magnesium silicate ($Mg_2S_iO_4$) are reacted to form the synthetic and purer form of AMS, $Al_2Mg_3(SiO_4)_3$: {$Al_4(SiO_4)_3$ + $3Mg_2SiO_4$ = $2Al_2Mg_3(SiO_4)_3$}. To this formulation, dextrose monohydrate was added to act as a carrier and he named the formulation, Medicinal Synthetic Aluminum Magnesium Silicate (MSAMS) [6]. MSAMS has proved effective against viral diseases and abnormal-cell diseases in both man and animals [7] It has adjuvant efficacy [8]. Despite these findings, the tissue kinetic parameters of MSAMS has not been studied in both man and animals.

Therefore, this study is designed to investigate the tissue kinetics of MSAMS in broilers.

Materials and Methods

The drug used for the study is Medicinal synthetic aluminum magnesium silicate (MSAMS) was supplied by Prof. MCO Ezeibe who has the patent.

Experimental animals

Thirty eight (38) day old broilers were purchased from a reputable hatchery and raised on deep litter until they are six weeks old. Feed and water were provided for them, ad libitum. They were vaccinated against Newcastle and gomboro.

Drug administration

A single dose of 50 mg/kg MSAMS was administered orally to the birds.

Sample collection: Tissue kinetics

Two birds were sacrificed at 120, 240, 360 and 480 hours PT for their livers, brains, kidneys, hearts and skeletal muscles which were rinsed with normal saline to remove blood and Homogenized using distilled water and placed in plastic bags to be stored at –10^0c until analyzed.

Preparation of MSAMS standard

Concentration of MSAMS in the formulation is 186 mg/g and its recommended dosage is 50 mg/kg.

Determination of MSAMS by Atomic absorption spectrophotometer (AAS)

Sample digestion

Homogenized tissue samples (0.5–1 g) were digested using wet acid digestion. Briefly, 5 mL of concentrated nitric acid (HNO_3) was added and heated at 80–120°C until a clear solution was obtained. For complete digestion, particularly of tissue samples, 1–2 mL of perchloric acid ($HClO_4$) was added, and heating continued until a clear, colorless digest was achieved.

The digests were cooled, filtered where necessary, and diluted to a known volume (50 mL) using deionized water [9].

Preparation of standard solutions

Standard stock solutions of aluminum and magnesium and silicon were prepared and serially diluted to obtain working standards of varying concentrations (0, 1, 2, 5, and 10 ppm). These standards were used to generate calibration curves for quantification.

Determination of aluminum and magnesium

Aluminum and magnesium concentrations were determined using an atomic absorption spectrophotometer (AAS) (PerkinElmer). Appropriate hollow cathode lamps were used, and the instrument was operated at wavelengths of 309.3 nm for aluminum and 285.2 nm for magnesium using an air–acetylene flame. The instrument was calibrated using blank and standard solutions before sample analysis.

Absorbance readings were obtained, and concentrations of metals in plasma and tissue samples were calculated using the calibration curve and expressed as mg/L (plasma) or mg/g (tissue).

Calibration curves were prepared using standard solutions, and sample concentrations were calculated accordingly [9].

Determination of silicate (Colorimetric Method)

Silicate concentration in plasma and tissue samples was determined using the molybdenum blue colorimetric method, a widely accepted technique for silicon analysis.

Procedure

An aliquot of the digested sample was taken, and ammonium molybdate reagent was added under acidic conditions to react

with silicate, forming a yellow silicomolybdic acid complex. This complex was subsequently reduced using a suitable reducing agent (e.g., ascorbic acid) to form a blue-colored complex (molybdenum blue) [9].

The intensity of the blue color, which is directly proportional to the silicate concentration, was measured spectrophotometrically at a wavelength of approximately 810–820 nm.

A calibration curve was prepared using standard silicate solutions, and the concentration of silicate in the samples was determined from the curve.

Calculation of concentrations

Metal and silicate concentrations were calculated using calibration curves and appropriate dilution factors. Results were expressed as: mg/g for tissue.

Concentration in sample = AAS reading x dilution factor

Sample weight or volume

Basic pharmacokinetics parameters

Pharmacokinetic analysis

Pharmacokinetic parameters were determined using the non-compartmental method based on statistical moments theory [10] and calculated using well-established equations [11].

Statistical analysis

The data on plasma kinetics and pharmacokinetic parameter were presented in graphical and tabular form and as MeanStandard Error of Mean (SEM) and the means between each time interval compared by Repeated Analysis of Variance (ANOVA). Tested for significant differences by Turkey Post hoc test and least significant difference was judged at 5% ($P \leq 0.05$): [12].

Results

Medicinal synthetic aluminum magnesium silicate (MSAMS) concentration in the brain of broilers administered aluminum magnesium silicate are shown in table 1. The highest concentration of 0.72 ± 0.10 mg/g was obtained at 120 hours in the broilers administered medicinal synthetic aluminum magnesium silicate. These concentrations subsequently decreased and at 480 hrs post drugs administration, the MSAMS levels was 0.24 ± 0.02 mg/g in broilers. The concentrations of MSAMS obtained at various time periods post drugs administration were significantly ($p < 0.05$) lower in the brain of broilers. Peak concentrations of 2.20 ± 0.28 mg/g medicinal synthetic aluminum magnesium silicate was obtained from the heart of broilers treated with MSAMS at 240 hr post treatment. These amounts decreased to 1.65 ± 0.27 mg/g at 360 hr post drug administration and later increased to 1.81 ± 0.17 mg/g at 480 hr post drug administration. The peak concentration of MSAMS at 240 hr PT in the liver of broilers treated with medicinal synthetic aluminum magnesium silicate was 2.51 ± 0.36 mg/g and later decreased to 2.10 ± 0.20 at 480 hours post treatment. Means of MSAMS concentrations in the kidney of treated broilers was 1.31 ± 0.21 at 120 post drug administration but this concentrations continually increased to 2.89 ± 0.38 up to 480 hours post drug administration instead of decreasing. The concentrations of MSAMS in the skeletal muscles of treated broilers was 2.41 ± 0.13 at 120 hours post drug administration. At 240 hours, the concentrations reduced to 1.14 ± 0.06 and later increased to 3.04 ± 0.14 at 480 hours post drug administration. The concentrations of MSAMS in the skeletal muscles of treated broilers was 2.41 ± 0.13 at 120 hours post drug administration. At 240 hours, the concentrations reduced to 1.14 ± 0.06 and later increased to 3.04 ± 0.14 at 480 hours post drug administration. The concentrations of MSAMS in the broilers at various time periods were significantly ($p<o.o5$) different as shown in table 1.

Time (hr) **Tissue (mg/g)**	**120**	**240**	**360**	**480**
Brain	0.72 ± 0.10	0.52 ± 0.05	1.39 ± 0.11	0.24 ± 0.02
Heart	0.51 ± 0.06	2.20 ± 0.28	1.65 ± 0.27	1.81 ± 0.17
Liver	2.41 ± 0.23	2.51 ± 0.36	2.18 ± 0.07	2.10 ± 0.20
Kidney	1.31 ± 0.21	1.38 ± 0.08	2.16 ± 0.17	2.89 ± 0.38
Skeletal muscle	2.41 ± 0.13	1.14 ± 0.06	1.26 ± 0.06	3.04 ± 0.14

Table 1: The average medicinal synthetic aluminum magnesium silicate concentrations (mg/g) in the tissues of broilers treated with MSAMS (50 mg/kg).

Tissue	k_el (min^{-1})	t½ (hours) ± SEM
Heart	-0.003 ± 0.002	N/A
Liver	+0.001 ± 0.000	1501.00 ± 641
Brain	0.002 ± 0.003	360.00 ± 284
Kidney	-0.002 ± 0.000	N/A
Muscle	0.056 ± 0.002	N/A

Table 2: Elimination rate constants (h^{-1}) and Elimination Half Lives ($T_{1/2/hr}$) of medicinal synthetic aluminum magnesium silicate in various tissues of broilers treated with MSAMS.

Discussion

Dextrose monohydrate helped AMS absorption through these pharmacokinetic mechanisms: The observed medicinal synthetic aluminum magnesium silicate (MSAMS) tissue concentration profile suggests that dextrose monohydrate may have enhanced the oral absorption of MSAMS by providing a rapidly soluble carbohydrate matrix that supported gastrointestinal uptake. Glucose is absorbed in the small intestine through specific transport mechanisms, particularly sodium-dependent glucose transport, and this process is associated with the movement of water and solutes across the intestinal epithelium [13]. Accordingly, the rise in tissue concentration, with a peaks at 480 h, indicates that MSAMS was rapidly absorbed following administration and slowly distributed to tissues. This finding is consistent with the view that dextrose monohydrate functioned as a suitable vehicle for improving the availability of MSAMS for intestinal transport and systemic entry. The subsequent decline in concentration after the peak, with minor fluctuations at later time points, may reflect distribution and elimination processes following absorption. Overall, the formulation of MSAMS with dextrose monohydrate appears to have supported early absorption and systemic exposure, although the extent of this effect may have varied with dextrose concentration. So, in general, dextrose monohydrate incorporated into MSAMS formulation enhanced AMS gastrointestinal absorption through particle dispersion, osmotic transit acceleration, and solid dispersion solubilization, accounts for peak concentrations of MSAMS in sampled tissues hours PT. This represents substantial bioavailability improvement for poorly soluble silicates.

The presence of medicinal synthetic aluminum magnesium silicate (MSAMS) concentrations in the brain, skeletal muscle, liver, kidney and heart of the broilers shows that msams was absorbed though not as a single entity (MSAMS) but in dispersed forms (Al, Mg and Si) and readily distributed to the tissues and organs. This findings agrees with [6] who stated that incorporating dextrose monohydrate in synthetic AMS formulation would make it absorbable into systemic circulation. The presence of MSAMS for up to 480 hours (20 days) post drug administration in the tissues of broilers in this study is an indication that the drug administered orally is not eliminated in broilers within 20 days.

The highest accumulation of MSAMS in the sampled tissues was found to be in the skeletal muscle and kidney of the treated broilers. This finding could suggest that msams slowly accumulates and are slowly released in and from these tissues thereby delaying elimination. This is evidenced by peak concentrations of 3.04 ± 0.14 mg/g and 2.89 mg/g which were obtained at 480 hours post drug administration muscle and kidney respectively. [14] supports this findings about AMS. The lowest concentration of msams was found to be in the brain of treated broilers. This finding could suggest that the distribution of msams to the brain was inhibited by tight junctions at the blood brain barriers [11]. The high concentrations of msams in the liver and kidney of broilers are expected in that the liver is the main organ of biotransformation, while kidney is the primary organ of excretion [15]. The msams concentration in the heart of broilers indicates substantial uptake and retention of nanomaterial in the myocardium. This stable cardiac buffering (4.4% dose recovery at peak) ensures sustained cardio protection against heat stress-induced oxidative damage and other related metabolic conditions [16].

With negative elimination rate constant in sampled tissues (heart, kidney, muscle), it means that there is no clear elimination phase in heart, kidney and skeletal muscle because at 20 days post drug administration MSAMS nanomaterial were still accumulating or distribution and redistribution was still ongoing in these tissues This could also suggest that a single dose of 50 mg/kg MSAMS can stay for up to one month in the tissues and organs of broilers. Furthermore, the presence of MSAMS Nano material for up to 20 days post drug administration indicates that the withdrawal period for medical synthetic aluminum magnesium silicate is beyond 20 days post drug administration.

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