國立中興大學 National Chung Hsing University & NSP 矽牧公司 Si Moon

# NSP for Life !

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(友善生命之"物理作用"衍生多重功能)

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無抗生素及化學藥物之畜產養殖優質化

# 力克靈

## 台灣發明 世界首創

### 天然矽片 NSP (Natural Silicate Platelets)

### 力克靈-非屬飼料或飼料添加物

[天然矽片]採自天然界礦土，2003中興大學發明--奈米脫層技術製造矽片; 於2011~2022年間經多領域專家教授(林江珍/陳洵一/林子恩等)開發畜產應用，進一步發現矽片多層功能: (1) “物理吸附性”--因其特殊幾何形狀(薄片狀)，每公克矽片具有750平方公尺高表面積覆蓋力，又具有陰離子電荷性，可以表現出”物理性捕捉”同時抑制微生物繁殖生長，另外可”吸附”毒素.重金屬.氨氣及硫化合物等功能, (2)”無毒性”--矽片本身並無毒性，亦不造成抗藥性，適合廣泛使用於家禽及環境，平衡微生物菌落, (3)”長效性”--矽片具長期隱定特性:本身不被化學分解，可長效性存在且”友善地參與大自然平衡”，降低污染危害及復原環境生機。

NSP並非化學藥物，其”複合型”功能特點，為學術突破性的應用創新。又經興大多位專家教授歷經10年以上應用研發，才慎重於2022首次商業化以期貢獻台灣畜產業，尤其在此”後抗生素時代”及減少化學藥物使用之大趨勢下，”NSP之物理效應”對食品安全及優質養殖提供新解方，更顯重要。

*力克靈(NSP配方)，依據實驗結果，能阻止原蟲，細菌及病毒等微生物繁殖，吸附臭味氣體，減少呼吸道/腸道感染，避免疾病發生，增進家畜，家禽及水產動物健康。*

# 論文研究發表

(Lin and Peng, ACS Applied Materials and Interfaces, 2 (6), **2010**, 1608)

ARTICLE

## Evaluation on Cytotoxicity and Genotoxicity of the Exfoliated Silicate Nanoclay

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**ABSTRACT** The concern about toxicity for nanosilicate platelets (NSP) derived from natural montmorillonite clay is addressed. The NSP nanoclay was isolated from polyamine−salt exfoliation of the layered silicate clay into randomized individual plates, possessing multiple ionic charges on the surface of silicate plates with an average geometric dimension of ca. 80 × 80 × 1 $nm^3$. The material had been previously shown to be effective for antimicrobial and tendency for adhering onto the biomaterial surface based on the direct observation by using scanning electron microscope. The material safety on genotoxic effect was investigated by using three different test systems: the Comet assay test on Chinese Hamster Ovary (CHO) cells in vitro, micronucleus (MN) assay in vivo and the *Salmonella* gene mutation assay on strain TA98, TA100, TA102, TA1535 and TA1537. The Comet assay showed no DNA damage after 24 h of incubation with NSP of 1000 μg/mL. The MN test indicated no significant micronucleus induction in the CHO cells at the concentrations tested. With all five strains of *Salmonella typhimurium*, none of mutations was found. Furthermore, cytotoxicity of the same material was assayed by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and lactate dehydrogenase (LDH) release, showing a low cytotoxicity on CHO cells below 1000 μg/mL after 12 h incubation period and a dose-dependent effect after 24 h incubation. For feeding to rats, the acute oral toxicity was shown a low lethal dose ($LD_{50}$) or greater than 5700 mg/kg body weight for both male and female Sprague-Dawley rats. Overall, the study has demonstrated the safety of the NSP for potential uses in biomedical areas.

**KEYWORDS:** nanosilicate platelets • cytotoxicity • genotoxicity • nanomaterials • acute oral toxicity

**NSP"矽片" -- 安全性及無毒性測試：**

1. **老鼠急毒性：= 食鹽**
2. **細胞毒性： < 1000 ppm**
3. **基因毒性：無**
4. **人類細胞：促進生長癒合**

The safety of NSP with respect to cytotoxicity and genotoxicity has been evaluated.

1. A low lethal dose (**$LD_{50}$ > 5,700 mg/kg or similar to NaCl**) was found.
2. Low cytotoxicity (1000 ppm on CHO cells) and none of genotoxicity were reported.

(Journal of Physical Chemistry C (2011) 115, 18770)

THE JOURNAL OF PHYSICAL CHEMISTRY C

ARTICLE

pubs.acs.org/JPCC

# Inhibition of Bacterial Growth by the Exfoliated Clays and Observation of Physical Capturing Mechanism

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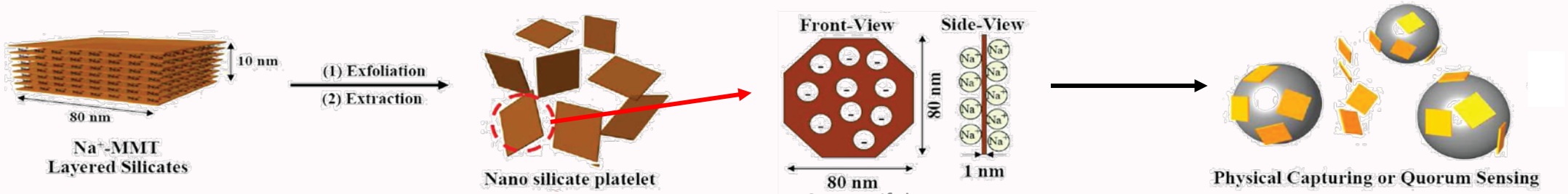
**ABSTRACT:** We observed unexpected antimicrobial behavior from the silicate platelets, prepared from the exfoliation of natural clays, for a broad spectrum of microorganisms. The antimicrobial properties are attributed to the unique structure of the exfoliated platelets, which possess an average dimension of 80 nm × 80 nm × 1 nm and polyvalent ionic charges (ca. 18 000 sodium ions/platelet) on the surface of ultrathin platelets. The thin shape and ionic character of the silicates enables them to physically adhere to microbe surfaces and be directly observed by scanning electron microscopy. The nanometer-sized thin silicates with the uniquely combined features of large surface areas and polyvalent charges have potential uses for biomedical treatments.


NSP物理捕捉圖示: 微生物對談訊號被NSP捕捉而抑止其繁殖! physical capturing or blocking "Quorum Sensing" of bacterial cross-talking signals -- 物理性捕捉"群感效應"或對談機制!



# NSP以物理作用抵抗病毒感染 (動物實驗)
# Including JEV, dengue and influenza A virus

(Hsu, Lin and Lin, Journal of Virology, 88, 2014, 4218)

JVI Journals.ASM.org

**2014 我們發表一篇重要的論文! NSP 可以物理性吸附/抵抗病毒的入侵**

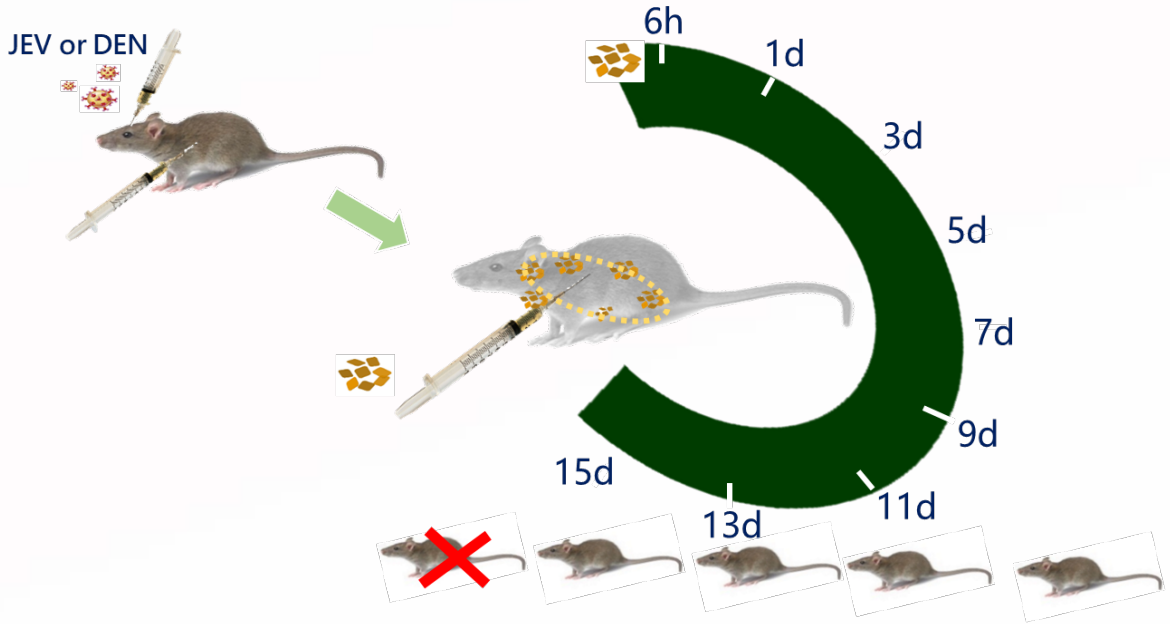
## Surfactant-Modified Nanoclay Exhibits an Antiviral Activity with High Potency and Broad Spectrum

Jian-Jong Liang,[a] Jiun-Chiou Wei,[b] Yi-Ling Lee,[a] Shan-hui Hsu,[b] Jiang-Jen Lin,[b] Yi-Ling Lin[a,c]

Institute of Biomedical Sciences[a] and Genomics Research Center,[c] Academia Sinica, Taipei, Taiwan; Institute of Polymer Science and Engineering, National Taiwan University, Taipei, Taiwan[b]

**ABSTRACT**

Nanomaterials have the characteristics associated with high surface-to-volume ratios and have been explored for their antiviral activity. Despite some success, cytotoxicity has been an issue in nanomaterial-based antiviral strategies. We previously developed a novel method to fully exfoliate montmorillonite clay to generate the most fundamental units of nanoscale silicate platelet (NSP). We further modified NSP by capping with various surfactants and found that the surfactant-modified NSP (NSQ) was less cytotoxic. In this study, we tested the antiviral potentials of a series of natural-clay-derived nanomaterials. Among the derivatives, NSP modified with anionic sodium dodecyl sulfate (NSQc), but not the pristine clay, unmodified NSP, a silver nanoparticle-NSP hybrid, NSP modified with cationic *n*-octadecanylamine hydrochloride salt, or NSP modified with nonionic Triton X-100, significantly suppressed the plaque-forming ability of Japanese encephalitis virus (JEV) at noncytotoxic concentrations. NSQc also blocked infection with dengue virus (DEN) and influenza A virus. Regarding the antiviral mechanism, NSQc interfered with viral binding through electrostatic interaction, since its antiviral activity can be neutralized by Polybrene, a cationic polymer. Furthermore, NSQc reduced the lethality of JEV and DEN infection in mouse challenge models. Thus, the surfactant-modified exfoliated nanoclay NSQc may be a novel nanomaterial with broad and potent antiviral activity.

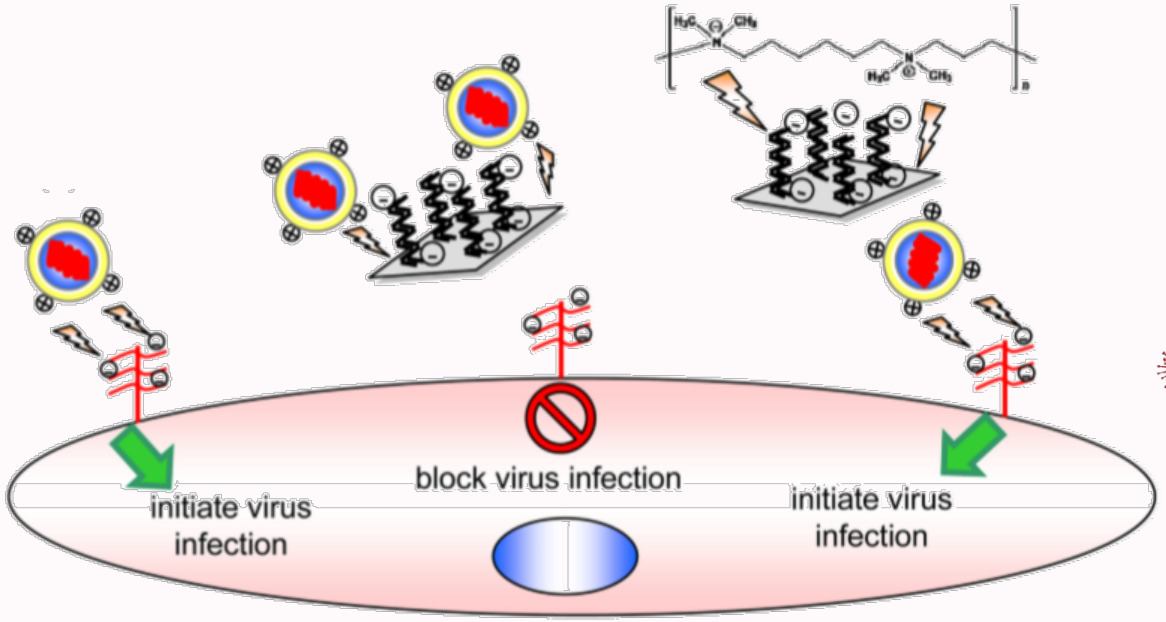



1. 注射NSP後, 病毒感染老鼠之存活率, 可從(0-20%)提昇至 (80-100%).
2. 解剖分析: NSP對肝臟安全性測試 ---無損害!

動物實驗: NSP在病毒感染前或者感染後,均可降低感染老鼠之死亡率,有效性高達80-100% !
而且NSP具有高"治療指數" (therapeutic index), 即安全性或無毒性!

# NSP “物理盾牌效應”抗病毒機制圖 (非化學性)

(Surfactant- modified nanoclay exhibits an antiviral activity with high potency and broad spectrum, *Journal of Virology, 88, 4218-4228.)*



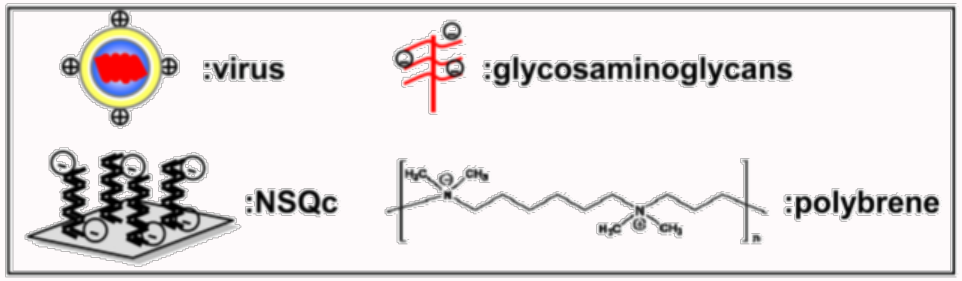
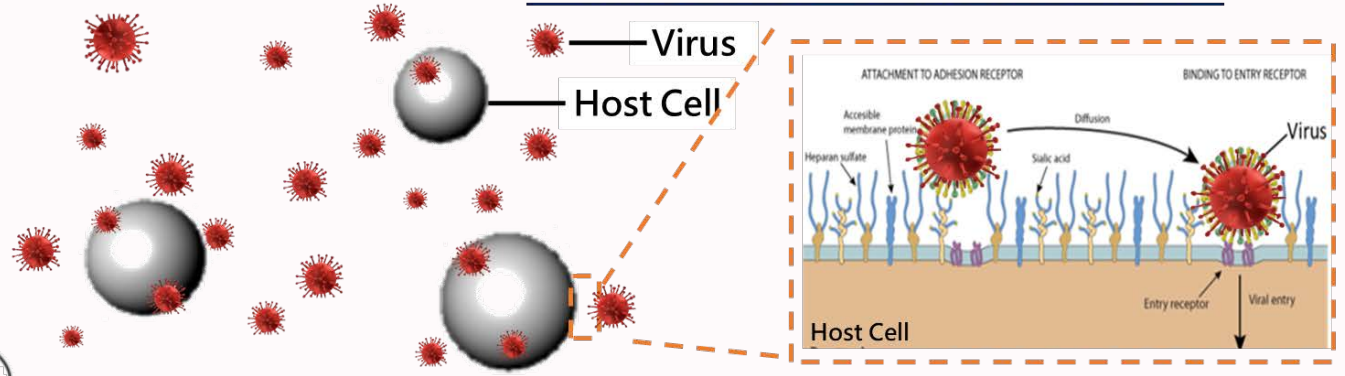
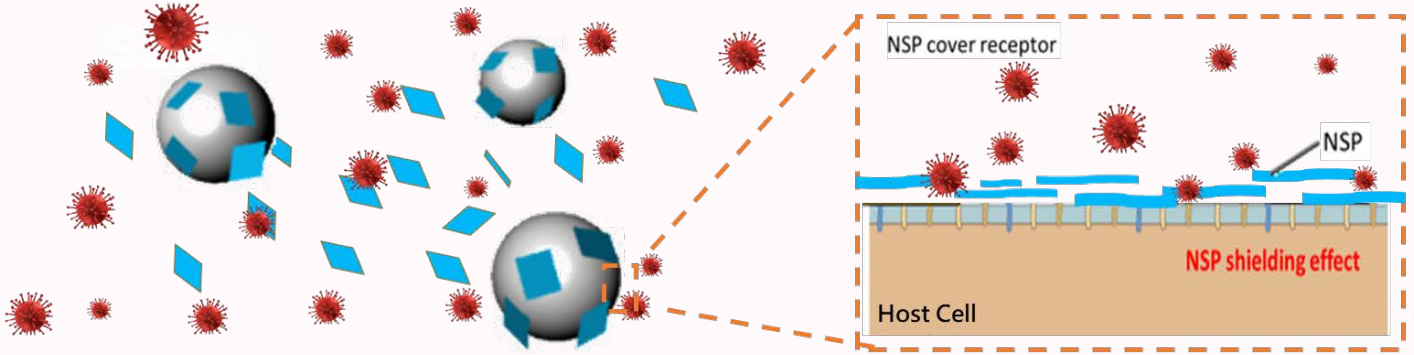




示意圖: 一般病毒入侵正常細胞之感染過程

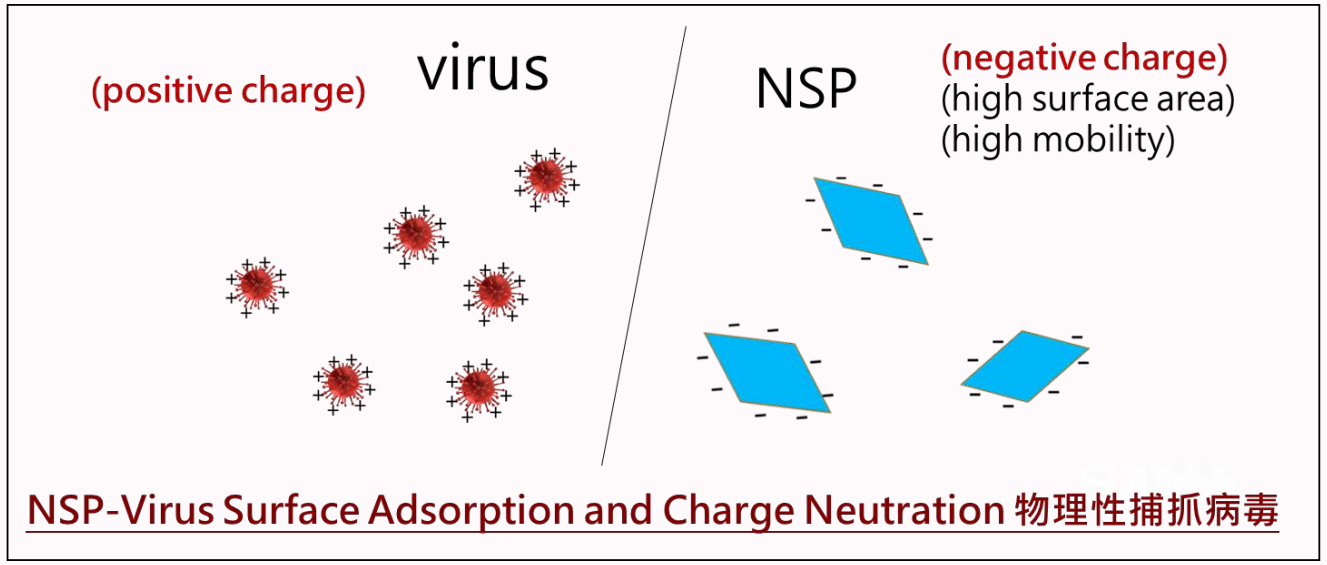



NSP“盾牌屏蔽”物理性捕捉病毒,阻斷病毒接觸細胞表面受體

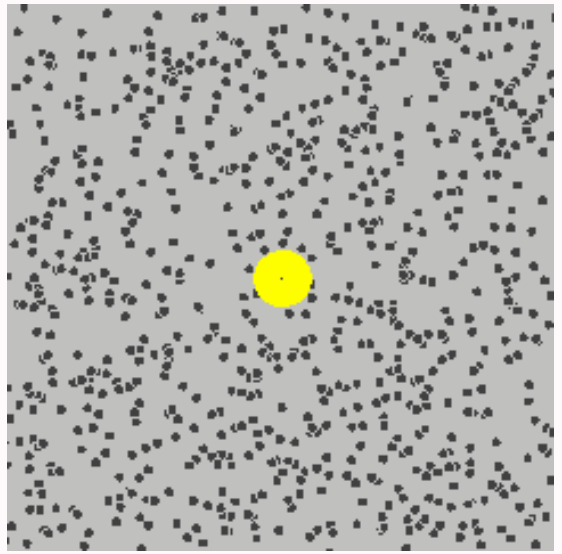


# NSP物理性抗病毒之基本原理--(非化學性)
# (the basic principle of NSP anti-virus)

1. NSP high surface area 高表面積
2. Positive/Negative charge neutralization高正電荷吸附病毒(正負相吸)
3. NSP high mobility in water and in air 快速運動尋找病毒(快速布朗運動)
4. In vitro and in vivo (JEV, DEN and influenza A virus) 流感、日本腦炎、登革熱3種病毒證明有效性



NSP-Virus Surface Adsorption and Charge Neutration 物理性捕抓病毒



*JJ Lin, Yi-Ling Lin*,et al. **2014.** Surfactant- modified nanoclay exhibits an antiviral activity with high potency and broad spectrum, Journal of Virology, 88, 4218;* *(Taiwan Patent I546080 (2013)*

*JJ Lin et. al., 2011. Inhibition of Bacterial Growth by the Exfoliated Clays and Observation of Physical Capturing Mechanism, Journal of Physical Chemistry C, 115, 18770181.*

# NSP--沙門桿菌感染(雞.豬飼料/飲水)禽流感及細菌感染

(International Journal of Nanomedicine, 7, **2012**, 2421-2423)

International Journal of Nanomedicine

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ORIGINAL RESEARCH

## Efficacy and safety of nanohybrids comprising silver nanoparticles and silicate clay for controlling *Salmonella* infection

This article was published in the following Dove Press journal:
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11 May 2012
Number of times this article has been viewed

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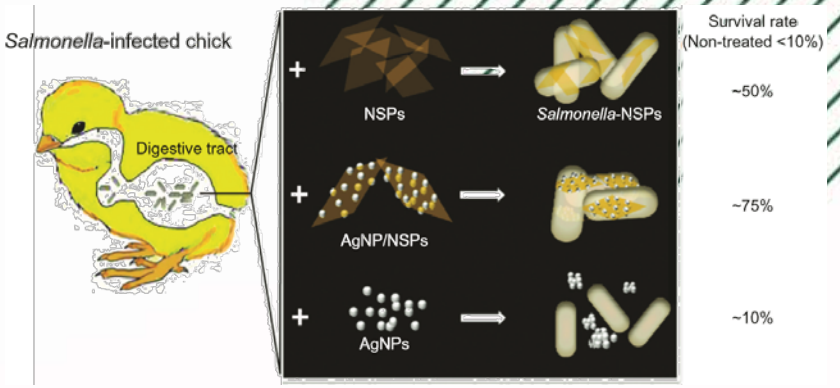
**Abstract:** Developing effective and safe drugs is imperative for replacing antibiotics and controlling multidrug-resistant microbes. Nanoscale silicate platelet (NSP) and its nanohybrid, silver nanoparticle/NSP (AgNP/NSP), have been developed, and the nanohybrids show a strong and general antibacterial activity in vitro. Here, their efficacy for protecting *Salmonella*-infected chicks from fatality and septicemia was evaluated. Both orally administrated NSP and AgNP/NSP, but not AgNPs alone, effectively reduced the systemic *Salmonella* infection and mortality. In addition, quantitative Ag analyses demonstrated that Ag deposition from AgNP/NSP in the intestines was less than that from conventional AgNPs, indicating that the presence of NSP for immobilizing AgNPs reduced Ag accumulation in tissue and improved the safety of AgNPs. These in vivo results illustrated that both NSP and AgNP/NSP nanohybrid represent potential agents for controlling enteric bacterial infections.

**Keywords:** silver, nanoparticle, biocompatibility, infection, cytotoxicity




- NSP and AgNP/NSP, but not AgNPs alone, were potential antimicrobial agents for controlling **enteric bacterial infection.**
- In contrast to the considerable Ag deposits, **the Ag accumulation in digestive tissues from AgNP/NSP was significantly decreased**, showing improved **safety** over conventional AgNPs in animals.
- **降低雛白痢致死率50%**
- **提高抗生素對雛白痢療效70%**

# NSP--畜產飼料添加去除毒素-伏馬菌素FB1

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Article

pubs.acs.org/JAFC

## Evaluation of Efficacy and Toxicity of Exfoliated Silicate Nanoclays as a Feed Additive for Fumonisin Detoxification

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Supporting Information

**ABSTRACT:** The efficacy of nanosilicate clay platelets (NSCP), exfoliated silicates from natural montmorillonites, as a feed additive for ameliorating fumonisin B1 (FB1) toxicosis was evaluated. Toxicological mechanisms by NSCP were examined through proteomic and biochemical analyses. Dietary supplementation with NSCP at a low level of 40 mg/kg of feed improved growth performances in chickens with respect to FB1 toxicosis. Other issues of ameliorated symptoms including serum and/or hepatic aspartate aminotransferase activity, oxidative stress indicators, and sphinganine/sphingosine ratio, a hallmark of FB1 toxicosis, were considered. Chickens with NSCP inclusion alone at 1000 mg/kg of feed exhibited no changes in hepatic histology, oxidative status, and serum parameters and even had a higher feed intake. Proteomic analysis with liver tissues identified 45 distinct proteins differentially affected by FB1 and/or NSCP, in which proteins involved in thiol metabolism and redox regulation, glycolysis, carcinogenesis, and detoxification by glutathione *S*-transferase were promoted by FB1, whereas NSCP caused differential changes of protein abundances related to methionine/cysteine and choline/glycine interconversion for glutathione synthesis, redox regulation by peroxiredoxin, toxin/metabolite delivery by albumin, glycolysis, tricarboxylic acid cycle, adenosine triphosphate (ATP) synthesis, and chaperon escort for endoplasmic reticulum stress relief. Functional analyses confirmed the enhancement of hepatic metabolic processes for ATP and NAD(P)H production to meet the need for detoxification, antioxidative defense, and toxin/metabolite clearance by FB1 or NSCP ingestion. On the basis of the amelioration of FB1 toxicosis, global profile of hepatic protein expressions, and validated toxicological mechanisms, NSCP were concluded as a safe and effective agent for FB1 detoxification.

**KEYWORDS:** *nanosilicate platelets, fumonisin, detoxification, liver, proteomics*

- NSP(40 ppm)減緩毒素中毒雞隻生長遲滯 (by 10%)
- NSP亦有促進採食效果 (by 10.4%)
- In the study, dietary inclusion of NSP effectively improved the **growth performance and ameliorated FB1 toxicosis**, including oxidative stress, SA/SO ratio, and AST activity.
- Growth performances and toxicological analysis concluded NSP as a safe and effective agent for FB1 detoxification. Proteomic and function analyses suggested an enhancement of metabolic processes for ATP and NAD(P) H production for detoxification and antioxidative mechanisms, following toxin/metabolite clearance by NSP inclusion.

# 矽片(抗病毒)使用前後比較 (白蝦)

## 控制組

- ✓ 水質:魚池水質顏色較為混濁.
- ✓ 白蝦:無活力且蝦子表面較無色澤.

未添加

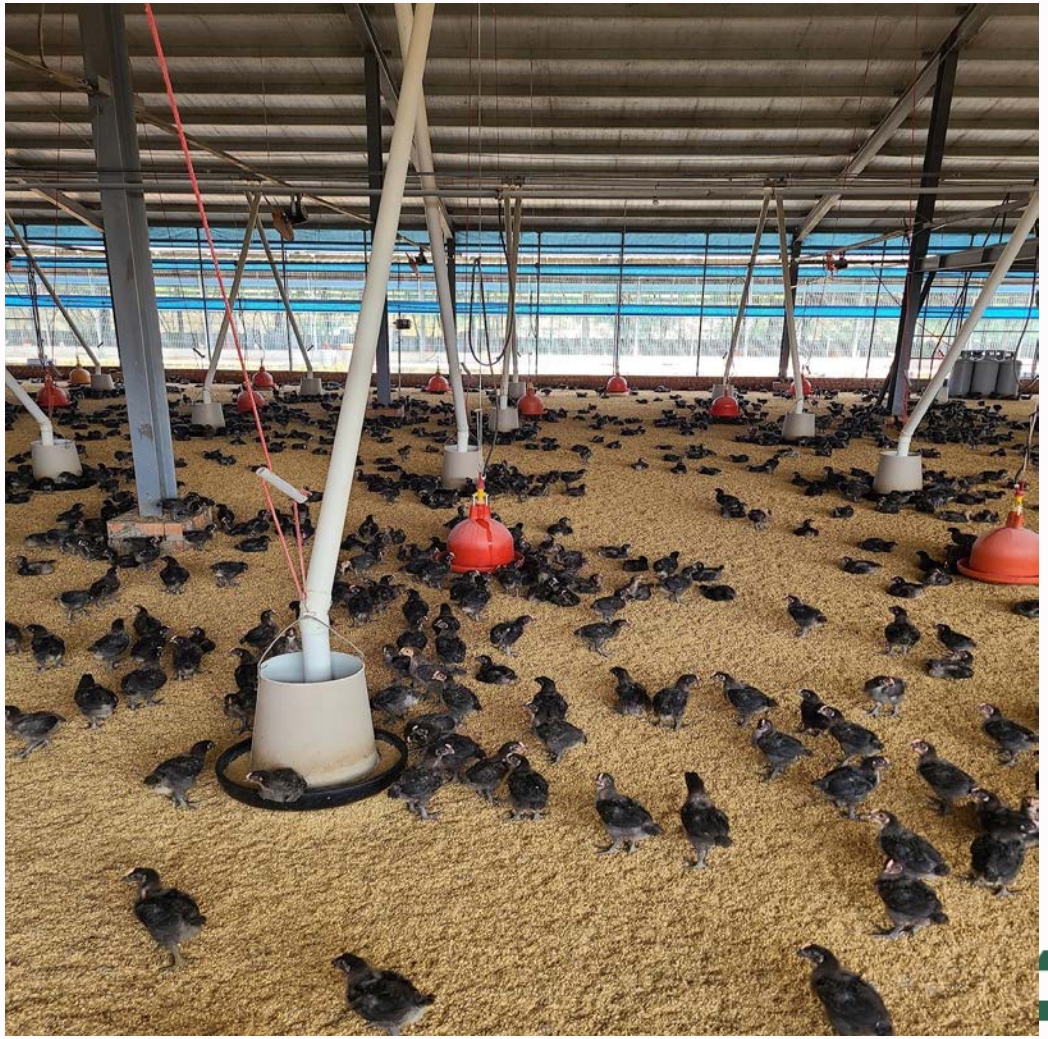
## NSP組

效果超越預期！(10 ppm預防病毒入侵)
(使用矽靈寶-c)

- ✓ 水質:魚池水質顏色較為清澈.
- ✓ 白蝦:有活力且身體顏色較為透明、光滑.

Day 2

# The disease of Coccidiosis (Chickens)—the cleaning and moisture of floor hygiene and odor of ammonia (NSP reducing the sporulation of coccidial oocysts in the life cycle)



# NSP 解決市場需求


01 取代抗生素、抑止傳染性疾傳播、去除毒素

02 促進生長、抗菌、抗病毒 (禽流感)、吸附黴菌毒素，節省飼料中添加劑成本約14-66%

03 可以去除湖泊水中微囊藻毒素，降低水源污染

1. **天然來源NSP產品--多功能，低單價，可量產， 高效益等市場競爭力.**
2. NSP 為創新原材料組成， 將取代化學藥物使用，增加食品安全，**為0→1創新**.

已有農委會核准非屬飼料添加物函文

# Livestock

## NSP-formulated LIN-KER-LIN

固態

### 力克靈-S

**Powder product**
**Registered in Taiwan Government**

液態

### 力克靈

**Liquid product Registered**





NSP For Life!

矽牧股份有限公司
Si Moon Company

# THANK YOU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