

CÔNG TY CỔ PHẦN TRƯỜNG VIỆT

Truongviet joint stock company



TRUONGVIET JSC

Thiết kế, tạo mẫu, chế thử, sản xuất và kinh doanh các trang thiết bị trường học các cấp học theo Thông tư của Bộ Giáo dục & Đào tạo và đồ chơi trẻ em mang tính giáo dục.

- ❖ Xây dựng cơ bản.
- ❖ Cung ứng dịch vụ tin học.
- ❖ Thiết kế, dàn dựng sân khấu, showroom bán hàng, hội chợ, triển lãm, hội nghị, hội thảo, phòng trưng bày, sự kiện, lễ hội.
- ❖ Thiết kế logo, thương hiệu và sản phẩm hàng hoá.
- ❖ Liên doanh, liên kết trên lĩnh vực xuất bản và văn hoá phẩm.
- ❖ Tạo mẫu và sản xuất các sản phẩm đóng gói (bao bì).
- ❖ Xuất nhập khẩu trực tiếp và ủy thác thiết bị và vật tư kỹ thuật.

Mẫu giáo



Tiểu học



Trung học cơ sở



Trung học phổ thông



Số 164, Tựu Liệt, xã Tam Hiệp, huyện Thanh Trì, Hà Nội.

* Tel/Fax: (024) 62 885 957 * Website: <http://truongvietjsc.com>

* Email: truongvietcp07@gmail.com

TẠP CHÍ

HÓA HỌC & ỨNG DỤNG

JOURNAL OF CHEMISTRY AND APPLICATION / TẠP CHÍ CỦA HỘI HÓA HỌC VIỆT NAM - ISSN1859-4069

Số 3B(70B)/5-2024

SỐ ĐẶC BIỆT

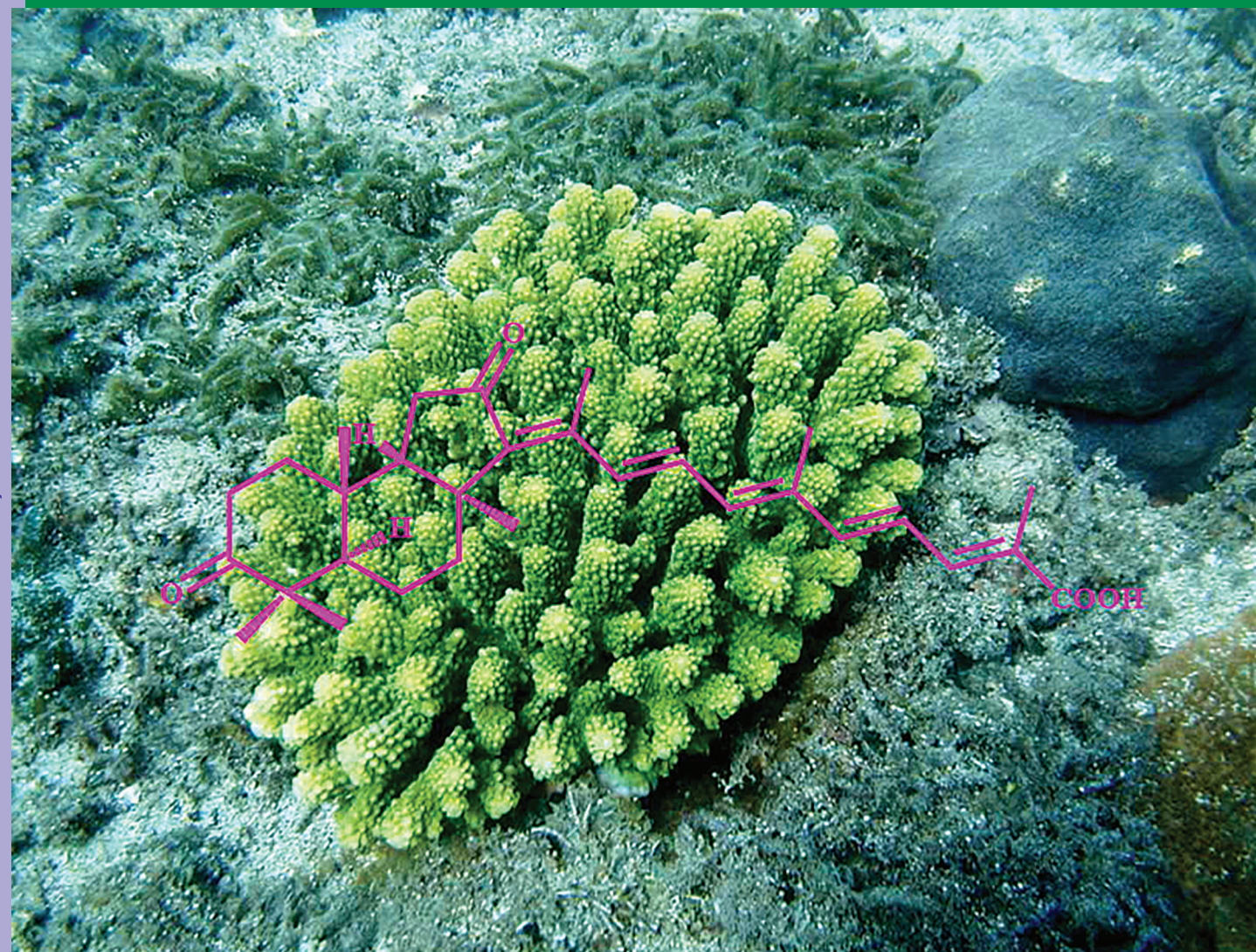
HỘI NGHỊ HÓA HỌC HỮU CƠ
TOÀN QUỐC LẦN THỨ X

(21 - 22/09/2024)

TẠP CHÍ HÓA HỌC & ỨNG DỤNG

HỘI NGHỊ HÓA HỌC HỮU CƠ TOÀN QUỐC LẦN THỨ X (20 - 22/09/2024)

SỐ ĐẶC BIỆT



HỘI ĐỒNG BIÊN TẬP

NGÔ QUỐC ANH, NGUYỄN CƯỜNG,
TRẦN THÀNH HUẾ, CHÂU VĂN MINH,
ĐẶNG VŨ MINH, TRẦN TRUNG NINH,
NGÔ ĐẠI QUANG, NGUYỄN ĐĂNG QUANG,
HỒ SĨ THOẢNG, NGUYỄN XUÂN TRƯỜNG,
VŨ VĂN TÂN

Phó Tổng Biên tập/Phụ trách Tổng Biên tập:
NGUYỄN HỮU ĐỨC

Thư ký tòa soạn:

LƯU THÚY HIỀN

Trình bày:

LÊ THANH HẢI

Tòa soạn:

164 đường Tự Liệt
xã Tam Hiệp, huyện Thanh Trì, Hà Nội
ĐT: (024) 62885957 - 0983 602 553
Email: tapchihoahocvaungdung@gmail.com
Tài khoản: 002704060000831
Ngân hàng Quốc tế-VIB, số 5, Lê Thánh Tông, Hà Nội.

Giấy phép xuất bản:

Số 319/GP-BTTTT
Bộ Thông tin và Truyền thông
cấp ngày 14/6/2016
In tại Công ty TNHH in ấn Đa Sắc
13 Ngọc Mạch - Xuân Phương
quận Nam Từ Liêm - Hà Nội

* Tạp chí xuất bản hàng quý,
phát hành vào các tháng 3, 6, 9 và 12.

Giá: 200.000 đồng

Trong số này:

3B(71)/9-2024

3 Design and synthesis of some novel amino acid derivatives containing benzo[d]thiazole

Nguyen Duc Du, Nguyen Van Dat,
Nguyen Thi Ngoc Mai, Ngo Lan Anh,
Do Quynh Anh, Nguyen Thu Phuong,
Bach Ngoc Lan, Pham Huu Dien, Duong Quoc Hoan

12 Flavonoids from *Combretum trifoliatum*

Nguyen Cong Thai Son, Le My Lam Thuyen,
Pham Nguyen Kim Tuyen, Huynh Bui Linh Chi,
Phan Nhat Minh, Nguyen Diep Xuan Ky, Bui Trong Dat,
Huynh Thi Kim Chi, Mai Dinh Tri, Dang Van Son,
Nguyen Kim Phi Phung, Nguyen Tan Phat

17 Glycosides from *Combretum trifoliatum*

Nguyen Cong Thai Son, Nguyen The Anh,
Nguyen Long Nguyen, Thong Ngoc Lan Anh,
Phan Nhat Minh, Nguyen Diep Xuan Ky,
Bui Trong Dat, Huynh Thi Kim Chi, Mai Dinh Tri,
Ngo Trong Nghia, Dang Van Son,
Nguyen Kim Phi Phung, Nguyen Tan Phat

23 Release of lovastatin drug from poly(lactic acid) biomaterial

Nguyen Thi Bich Viet, Vu Quoc Manh, Tran Thi Kieu
Giang, Doan Thi Yen, Vu Thi Thuong, Ha Manh Hung,
Nguyen Dang Dat, Vu Quoc Trung, Nguyen Ngoc Linh

31 Study on the effect of N/P ratio and cultivation conditions on biomass growth and phycocyanin production of cyanobacterium *Oscillatoria* sp. LBIOCTO

Dang Thi Mai, Bui Thi Thu Uyen,
Ba Thi Duong, Nguyen Thi Phuong Dung,
Luu Thi Thu Ha, Do Thi Cam Van,
Nguyen Thi Thu Phuong, Tran Dang Thuan

42 Three 3-benzylphthalide compounds isolated from the Moss *Erythrodontium julaceum* Paris

Nguyen Ngoc Khanh Van, Pham Nguyen Kim Tuyen

47 Copper-promoted directed amination of c-h bonds in benzamides to access 2-arylquinazolin-4(3h)-ones

Thanh T. V. Le, Ha T. T. Nguyen,
Nam T. S. Phan, Tung T. Nguyen

52 Total phenolic and flavonoid contents, and antioxidant capacity of Vietnamese *Curcuma Aromatica* Salisb

Bùi Mai Hoa, Lê Thị Minh Thúy, Lê Thị Huyền

- 58 Molecular docking and pharmaceutical studies of chromenoimidazocarboline derivatives as VEGFR-2 Kinase Inhibitors**
Dao Thi Nhung, Le Tuan Anh
- 66 Microwave-assisted three-component synthesis of new pyranonaphthoquinone derivatives**
Nguyen Ha Thanh, Nguyen Tuan Anh,
Le Nhat Thuy Giang, Nguyen Thi Quynh Giang,
Nguyen Van Ha, Nguyen Thi Nga, Nguyen Thi Hien,
Vu Duc Cuong, Dang Thi Tuyet Anh
- 72 Flavonoids from the aerial parts of *Oligoceras eberhardtii* gagnep. and their cytotoxic evaluation**
Nguyen Thi Binh Yen, Trieu Quy Hung,
Pham Van Cuong, Doan Thi Mai Huong,
Nguyen Thuy Linh, Tran Van Hieu, Nguyen Manh Hung
- 79 Palladium catalyzed, quinoline-based directed arylation of C–H bonds**
Hau C. Le, Danh T. Tran, Nam T. S. Phan, Tung T. Nguyen
- 84 Study on the preparation of lycopodiella cernua (L.) pic. capsules containing β -sitosterol and naringenin**
Thi Kim Tuyet Nguyen, Thi Thanh Mai Nguyen
- 89 Evaluating potential inhibitors of HEP-G2 from 14 new hydroxamate derivatives of lupane triterpenoids using molecular docking simulation and admet properties**
Dang Thi Tuyet Anh, Le Nhat Thuy Giang,
Nguyen Ha Thanh, Dao Thi Nhung
- 95 Structure - surface adhesion relationships of *e. coli* fimh proteins and mannosides: A molecular analysis of the main regulators**
Nguyen Ha Thanh, Pham Viet Ha Quang,
Nguyen Cam Linh, Pham The Hai
- 103 Preparation, characterization, and properties of some SiO_2 nanocomposite of polythiophenes containing hydrazone group**
Do Ba Dai, Nguyen Huu Thinh, Le Tien Dat,
Le Thanh Nhan, Bui Phuong Thao, Dong Thi Thu Hang,
Nguyen Ngoc Linh, Nguyen Thi Hong Nhung,
Vu Quoc Manh, Vu Quoc Trung
- 109 Characterization of acrylic coatings containing poly(triethylammonium 3-thiopheneacetate) polyelectrolyte and nano- SiO_2**
Nguyen Thi Hong Nhung, Nguyen Kim Loan,
Vu Quoc Trung, Bui Tuan Anh, Nguyen Ngoc Hai,
Vu Viet Bac, Nguyen Ngoc Linh
- 116 Các hợp chất geranylphenylacetate glycoside và triterpenoid từ cây *Aphanamixis polystachya***
Ngô Anh Bằng, Phạm Hải Yến, Bùi Hữu Tài,
Trương Thị Thu Hiền, Phan Văn Kiệm
- 123 Tổng hợp một số dẫn xuất mới từ madecassic acid có sự biến đổi cấu trúc vòng A**
Trần Văn Lộc, Nguyễn Thế Anh, Trần Văn Chiến,
Trần Tuấn Anh, Trần Thị Phương Thảo
- 129 Tổng hợp một số hợp chất lai coumarin-pyrimidine, coumarin-benzothiazepine đi từ các hợp chất α , β -ketone không no**
Dương Ngọc Toàn, Đinh Thuý Vân, Khouamai Luethor
- 134 Các hợp chất phenolic và lignan từ loài *Symplocos cochinchinensis***
Lê Thị Giang, Ninh Khắc Bản, Hoàng Trọng Dân,
Nguyễn Thị Thu Thủy, Vũ Mai Thảo, Nguyễn Thị Mỹ Ninh,
Nguyễn Thị Ánh Tuyết, Nguyễn Xuân Nhiệm
- 139 Nghiên cứu ứng dụng medium chain triglycerides (MCTS) trong công thức son dưỡng nhân sâm**
Bạch Hải Nghi, Vũ Trung Đức, Đào Huy Toàn
- 149 Nghiên cứu sử dụng phản ứng đa thành phần để tổng hợp các hợp chất dị vòng mới khung dihydronaphthofuran có chứa nguyên tố flo**
Nguyễn Hà Thanh, Hoàng Thị Phương,
Đặng Thị Tuyết Anh, Nguyễn Thị Quỳnh Giang,
Trần Văn Kết, Vũ Ngọc Doãn, Nguyễn Thị Loan,
Vũ Thị Thu Hà, Nguyễn Thị Kim Tuyết, Lê Nhật Thùy Giang
- 155 Nghiên cứu khả năng kháng oxy hóa và kháng vi sinh vật của cây cam thảo nam (*Scoparia dulcis* Linn)**
Nguyễn Thị Hoài Ngân, Văng Thị Kim Anh,
Đỗ Thị Huỳnh Như, Tôn Nữ Liên Hương
- 160 Tổng hợp và hoạt tính gây độc tế bào ung thư của một số hợp chất từ zerumbone**
Phạm Thế Chính, Phạm Thị Thắm, Hoàng Thị Thanh,
Vũ Thị Liên, Vũ Tuấn Kiên, Trần Thị Thu Phương,
Phan Thanh Phương, Nguyễn Thị Thao
- 166 Halosit gắn dopo ứng dụng nâng cao khả năng chống cháy và cơ tính của hệ composit polyetylen**
Hắc Thị Nhung, Nguyễn Hồng Thắm, Nguyễn Linh Chi,
Hồ Thị Oanh, Đoàn Tiến Đạt, Nguyễn Đức Tuyển,
Trần Quang Hưng, Trần Quang Vinh,
Nguyễn Văn Tuyển, Hoàng Mai Hà
- 173 Nghiên cứu phân lập và đánh giá hoạt tính chống oxy hoá của các flavonoid glycoside từ lá cây bình bát nước (*Annona glabra* L., annonaceae)**
Trần Thị Minh, Đỗ Minh Hiếu,
Trần Thị Minh Trang, Dương Hoàng Thúc
- 178 Nghiên cứu bào chế kem chống nắng với dịch chiết vỏ thanh long ruột đỏ (*Hylocereus costaricensis*)**
Phạm Diệu Linh, Trần Thu Hương, Lê Thị Thùy
- 183 Hàm lượng, thành phần, hoạt tính kháng vi sinh vật kiểm định và kháng viêm của các lớp chất lipid trong loài rong nâu *Lobophora australis* Z.sun, Gurgel & H.kawai**
Đào Thị Kim Dung, Nguyễn Thị Nga, Đặng Thị Minh Tuyết,
Trần Đình Thắng, Idania Rodeiro Guerra,
Ivones Hernández Balmaseda, Đoàn Lan Phương
- 191 Chế tạo hệ hạt nano tổ hợp chứa astaxanthin và curcumin: cải thiện khả năng phân tán, nâng cao tính ổn định và tăng cường hoạt tính chống oxy hoá**
Hồ Thị Oanh, Hắc Thị Nhung, Đoàn Tiến Đạt,
Quách Thị Quỳnh, Nguyễn Yến Thanh, Hoàng Mai Hà

- 197** Điều chế chất lỏng ion 1,4-diazabicyclo[2.2.2]octanium sol-gel làm xúc tác trong tổng hợp 4*h*-chromene
Nguyễn Thái Thế, Nguyễn Tấn Lực, Nguyễn Thị Huyền Trân, Phan Ngọc Hồng Thủy, Trần Hoàng Phương
- 207** Nghiên cứu chế tạo điện cực dựa trên vật liệu khung hữu cơ kim loại CuBTC và FeBTC ứng dụng trong cảm biến điện hoá phát hiện đồng thời amoxicillin và enrofloxacin với độ nhạy và độ chọn lọc cao
Đoàn Tiến Đạt, Phạm Thị Hải Yến, Nguyễn Thị Kim Ngân, Đoàn Tất Đạt, Trần Quang Hải, Hắc Thị Nhung, Hồ Thị Oanh, Nguyễn Đức Tuyền, Lê Quốc Hùng, Vũ Thị Thu Hà, Lê Thu Thảo, Hoàng Văn Hùng, Hoàng Mai Hà
- 213** Nghiên cứu tổng hợp hệ dẫn truyền thuốc plga-chitosan giúp cải thiện độ phân tán của diosmin
Tôn Anh Khoa, Trần Thị Trà Mi, Huỳnh Thị Kim Chi, Nguyễn Hoàng Phúc, Nguyễn Thị Cẩm Thu, Nguyễn Thị Hồng An, Hoàng Thị Kim Dung
- 219** Một số thành phần hoá học và hoạt tính gây độc tế bào ung thư của hợp chất thiophene từ loài *Pluchea indica* ở Việt Nam
Vũ Minh Trang, Trần Hoàng Anh, Phan Minh Giang, Đỗ Thị Việt Hương
- 223** Nghiên cứu chứng cất tinh dầu lá bạc hà (*Mentha arvensis*) thu hái ở tỉnh Quảng Nam và ứng dụng phối chế xà phòng
Cao Văn Miên, Nguyễn Đình Bảo Trân, Nguyễn Thúy Hằng, Nguyễn Hồng Khánh Phương, Trần Thị Ngọc Bích, Đỗ Thị Thúy Vân
- 229** Nghiên cứu sơ bộ thành phần hóa học loài *Camellia phanii* Hakoda & Ninh
Hoàng Thị Tuyết Lan, Nguyễn Việt Dũng, Vũ Thị Xuân, Bùi Thị Mai Anh, Nguyễn Thị Minh Hằng, Vũ Mai Thảo, Nguyễn Thị Mai
- 233** Các hợp chất triterpene glycoside khung (20s)-dammarane phân lập từ rễ cây Tam thất
Hoàng Văn Hùng, Lục Quang Tấn
- 242** Các hợp chất *cis*-clerodane furanoditerpenoid từ cây dây ký ninh (*Tinospora crispa*)
Nguyễn Văn Quốc, Bùi Hữu Tài, Phạm Hải Yến, Đan Thị Thuý Hằng, Lê Đức Giang, Phan Văn Kiệm
- 248** Các hợp chất flavonoid phân lập từ lá loài bùm bụp *Mallotus apelta*
Nguyễn Hoàng Anh, Vũ Kim Thư, Phạm Thế Chính, Nguyễn Xuân Nhiệm
- 253** Một số hợp chất terpenoid từ loài *Cryptolepis buchananii*
Nguyễn Đức Duy, Ngô Anh Bằng, Phạm Hải Yến, Đỗ Thị Trang, Nguyễn Thị Kim Thúy, Nguyễn Thị Cúc, Nguyễn Xuân Nhiệm, Phan Văn Kiệm, Ninh Khắc Bản, Bùi Hữu Tài
- 260** Tác dụng kháng viêm của Aurantiamide Acetate từ *Gomphrena Celosioides*: ức chế con đường tín hiệu Mapk trong tế bào Raw264.7
Ngô Văn Quang, Đặng Vũ Lương, Hồ Đức Cường, Đỗ Thị Thanh Xuân, Thành Thị Thu Thủy
- 266** Các dẫn xuất của acid caffeoylquinic từ loài phi điệp biển (*Suaeda maritima* (L.) Dumort.)
Bùi Thị Nha Trang, Bùi Hữu Tài, Bùi Thị Mai Anh, Nguyễn Thị Mai
- 271** Ứng dụng phương pháp phân tích sắc ký lỏng khối phổ phân giải cao LC-HR-QTOF-MS định lượng quercetin và kaempferol có trong dược liệu Hoàng Cầm (*Scutellaria baicalensis georgi*)
Nguyễn Thị Thúy Hằng, Trần Thị Yến, Nguyễn Thu Uyên, Đỗ Hoàng Giang, Ngô Quốc Anh
- 274** Khảo sát một số yếu tố ảnh hưởng đến quá trình ủ phân hữu cơ với than tro bay từ nhà máy nhiệt điện đốt than chất lượng thấp
Hoàng Thị Bích, Phạm Thị Hồng Minh, Trần Hữu Quang, Đỗ Tiến Lâm, Bùi Thị Thực, Hoàng Đại Tuấn, Phạm Cao Bách, Nguyễn Văn Trọng, Nguyễn Trọng Vinh, Nguyễn Trọng Vượng, Trần Quốc Toàn
- 281** Nghiên cứu carboxymethyl kappa-carrageenan bao bọc lectin từ rong đỏ *Kappaphycus striatus*
Hoàng Thị Trang Nguyễn, Lê Đình Hùng, Thành Thị Thu Thủy
- 288** Ba hợp chất flavonoid phân lập từ cỏ biển *Zostera marina* L.
Hồ Xuân Thủy, Huỳnh Tiến Thịnh, Đoàn Lan Phương, Phạm Nguyễn Kim Tuyền, Lê Đức Giang, Trần Đình Thắng

RELEASE OF LOVASTATIN DRUG FROM POLY(LACTIC ACID) BIOMATERIAL

NGUYEN THI BICH VIET¹, VU QUOC MANH², TRAN THI KIEU GIANG¹, DOAN THI YEN¹,
VU THI THUONG¹, HA MANH HUNG³, NGUYEN DANG DAT¹, VU QUOC TRUNG¹, NGUYEN NGOC LINH^{2,*}

1. Faculty of Chemistry, Hanoi National University of Education, 136 Xuan Thuy, Cau Giay, Hanoi, Viet Nam

2. Faculty of Pharmacy, Thanh Do University, Kim Chung, Hoai Duc, Hanoi, Viet Nam

3. Faculty of General Education, Hanoi University of Mining and Geology,
Duc Thang, Co Nhue, Bac Tu Liem, Hanoi, Viet Nam

*Email: nnlinh@thanhdown.edu.vn

SUMMARY:

Poly(lactic acid)/Lovastatin (PLA/Lov) biocomposites were successfully synthesized via the solution mixing method. The chemical structure, morphology, and thermal properties of lovastatin-carried biocomposites were characterized by Fourier Transform Infrared (FTIR) spectroscopy, Field emission scanning electron microscope (FESEM), and Differential Scanning Calorimetry (DSC), respectively. The results indicated that among 5 synthesized PLA/Lov biocomposites, PL10 with 10% wt. of Lov exhibited the most effective dispersion of lovastatin into the polymer matrix with a particle size in the range of 500–650nm. PL10 also exhibited the most uniform morphology and the smallest melting point (148.5°C). The release of lovastatin from PLA/Lov biocomposites in pH 2.0 and pH 7.4 buffer solutions was investigated using UV-Vis spectroscopy. The results indicated that the released lovastatin content was 27.26–40.58% and 32.73–54.25% after 30 hours of testing, respectively. Of the five biocomposites, PL10 showed the most reasonable results of drug release, with a lower release at pH 2.0 and a better release at pH 7.4, with a percentage of 27.26% and 54.25%, respectively.

Keywords: Poly(lactic acid)/lovastatin biocomposites, lovastatin release.

I. INTRODUCTION

According to the Biopharmaceutics Classification System (BCS), drugs are categorized into four types based on their solubility and permeability[1]. Among them, BCS class II drugs are characterized by high permeability but low aqueous solubility, which tends to limit drug absorption[2-4]. Research on drug formulations to improve the bioavailability of poorly soluble drugs by increasing their solubility and dissolution rate is one of the major challenges in the pharmaceutical preparation field. Poorly soluble drugs usually have a crystalline structure. Therefore, by developing new drug formulations, it is possible to change the crystalline structure to an amorphous form, improve the permeability by using hydrophilic carriers, and decrease the particle size[5-6]. There are several methods to enhance the drug solubility, such as (i) particle size reduction, (ii) nanosuspension, (iii) use of surfactants, (iv) salt formation, (v) use of prodrugs, (vi) pH adjustment, (vii) use of hydrotrope, (viii) solid

dispersion, (ix) bio-based nanocomposite fabrication, etc. [7-9]. Among them, bio-based nanocomposite fabrication is one of the most promising techniques to ameliorate drug solubility and bioavailability, and being environmentally friendly[10-14].

Lovastatin (Lov) is a well-known prescription drug in the statin class. It lowers blood fat by competitively inhibiting 3-hydroxy-3-methyl-glutaryl Co-enzyme A (HMG-CoA) reductase, reducing cholesterol synthesis in livers and decreasing cholesterol concentration in cells[15]. Lowering “bad” cholesterol and triglycerides and increasing “good” cholesterol helps reduce cardiovascular risks, preventing strokes and heart attacks. Lov exhibits poor bioavailability (<5%) due to its poor water solubility (0.4×10^{-3} mg/ml), low dissolution rate (53.9%), and short half-life (1-2 hours)[16-18]; therefore, regular medication is needed to maintain therapeutic levels in the blood[19]. There have been several studies on materials to improve the water solubility and bioavailability of Lov with a high degree

of oral absorption and extended delivery potential, such as Lov-containing phospholipid bilayers [20], Lov-carrying nanoparticles[21], or poly(lactic acid) microspheres[22]. Researchers also focused on the effects of the combined compositions and the ratios on the ability to control the Lov drug release in solutions simulating fluids and the human body, such as carrageenan/gellan gum[23], chitosan/alginate[24], chitosan/fish collagen [25],...

Poly(lactic acid) (PLA) is a versatile and environmentally friendly biopolymer that is widely applied in industrial fields such as packaging, textiles, disposable plastic tableware, etc., thanks to its thermoplastic behavior as well as its biodegradable, compostable, and recyclable properties.

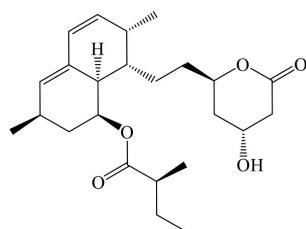
Especially, PLA is also known as a biocompatible material that emerged in various medical applications, from tissue generation[26], orthopedic[27], and cardiac[26] uses to drug delivery systems[28].

In this study, the solution mixing method was employed to prepare PLA/Lov biomaterial using PLA as a polymer matrix to disperse Lov while investigating the optimal ratio of Lov: PLA content by analyzing the structure, morphology, thermal properties, and drug release ability of the synthesized biocomposites. This work aimed to improve the solubility and release of Lov in two simulated solutions of gastric juice in the lower stomach and duodenum.

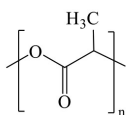
II. EXPERIMENTAL

2.1. Materials

Lov (white powder $\geq 98\%$) from Rhawn, China; PLA (solid, $M_w = 65,000\text{g/mol}$, melting point $264\text{-}269^\circ\text{C}$) from Sigma-Aldrich; and other chemicals including dichloromethane, ethanol, HCl, NaOH, KOH, and KH_2PO_4 supplied by Xilong Chemical Co. (China) were used without further purification. The structural formulas of Lov and PLA are shown below.



Lovastatin



Poly(lactic acid)

2.2. Preparation of PLA/Lov biomaterial

PLA/Lov biomaterial samples were prepared by the solution mixing method according to the procedure as follows: A Lov solution in 5 ml of ethanol was added slowly to a PLA solution in 12ml of dichloromethane while stirring at a speed of 2.10^4rpm . High speed supports increasing the capacity of the solution of Lov in the solution of PLA[29]. Next, the mixture continued to be stirred at a speed of 400rpm for 1.5 hours. The obtained solution was poured into a petri dish and allowed to evaporate naturally for 24 hours. By varying the Lov: PLA content ratio, different PLA/Lov biomaterial samples were obtained, as shown in Table 1.

Table 1: Symbols and the composition of the PLA/Lov samples

No.	Sample symbol	PLA content (g)	Lov content (g)
1	PL5	0.5	0.025
2	PL7	0.5	0.035
3	PL10	0.5	0.050
4	PL15	0.5	0.075
5	PL20	0.5	0.100

2.3. Characterization

A Thermo Nicolet Nexus 670 FTIR spectrometer was used to analyze the chemical structure and functional groups of the PLA/Lov biocomposites. The morphology of the biomaterial was recorded using an SEM Hitachi S-4800 scanning electron microscope. Thermal properties were characterized by a DSC-60 Plus Shimadzu.

The drug release of Lov from the PLA/Lov biomaterial was investigated by a YOKE UV1900 Double Beam UV-Vis absorption spectrophotometer with a calibration curve.

2.4. Establishing a calibration curve of Lov in two buffer solutions

Two buffer solutions were prepared: a pH 2.0 buffer simulating gastric juice in the lower stomach and a pH 7.4 buffer simulating small intestinal fluid in the duodenum area.

Dissolve 19.0mg and 26.3mg of Lov in 200ml of pH 2.0 and pH 7.4 buffer solutions, respectively. Dilute these two solutions to different concentrations of Lov and measure the absorbance of the diluted solutions at the maximum wavelength (λ_{max}). The results obtained are presented in Table 2.

Table 2: Absorbance of Lov solutions of different concentrations at pH 2.0 and pH 7.4

Dilution	pH 2.0		pH 7.4	
	C_{Lov} , mol/l	Absorbance, A	C_{Lov} , mol/l	Absorbance, A
x4	7.838×10^{-5}	0.161	10.85×10^{-5}	2.380
x6	5.266×10^{-5}	0.132	7.233×10^{-5}	1.708
x8	3.919×10^{-5}	0.114	5.425×10^{-5}	1.216
x10	3.135×10^{-5}	0.103	4.340×10^{-5}	0.996
x12	2.613×10^{-5}	0.096	3.617×10^{-5}	0.890
x16	1.960×10^{-5}	0.085	3.100×10^{-5}	0.679
x18	1.724×10^{-5}	0.079	2.712×10^{-5}	0.618

The data in Table 2 was subjected to a linear regression to obtain two calibration equations that express the dependence of the absorbance on the concentration of Lov released in solution, and the results are shown in Table 3. It

can be seen that the linearities of the two calibration curves are satisfied ($R^2 > 0.991$). Therefore, these equations can be used to determine the Lov content released from the biocomposite in the studied buffer solutions.

Table 3: Standard equations of absorbance vs. Lov concentration in pH 2.0 and pH 7.4 buffers

Buffer	λ_{max} (nm)	Standard equation	R^2 coefficient
pH 2.0	238.8	$A = 1325.7 C_{Lov} + 0.06$	0.9916
pH 7.4	239.6	$A = 21956.0 C_{Lov} + 0.04$	0.9951

2.5. Study on the effect of Lov content on the release of Lov drug from the PLA/Lov biomaterial

The release of Lov medicine from the PLA/Lov biomaterial was investigated in pH 2.0 and pH 7.4 buffers with a certain amount of PLA/Lov samples fixed in 0.2l of buffer solution and maintained at 37°C. Then the mixture was stirred at 400rpm. The absorbance of the solution was recorded every hour by taking out 5ml of solution, filtering, and measuring A at λ_{max} . Each time, 5ml of the corresponding buffer was added to keep the mixture

volume constant during the experiment. The experiment lasted from 1 hour to 30 hours and was repeated three times to obtain the average value of absorbance.

The Lov content present in the solution was determined using the corresponding standard equation above. The percentage of Lov drug released in time t (hours) is calculated according to the formula:

$$C_{Lov} (\%) = \frac{m}{m_0} \times 100\%$$

where C_{Lov} : the percentage of Lov drug released (%)
 m : the amount of Lov released (g)
 m_0 : the initial amount of Lov (g)

III. RESULTS AND DISCUSSION

3.1. Structure, morphology, and thermal properties of PLA/Lov biocomposites

3.1.1. FT-IR spectra of PLA/Lov biocomposites

The results of FTIR analysis for Lov, PLA, and biocomposite are presented in Figure 1 and Table 4. Both FTIR spectra of Lov and PLA show characteristic bands of -CH sp^3 at 2,994-2,865 cm^{-1} for stretching vibrations and 1,459-1,355 cm^{-1} for bending vibrations. Besides, the

stretching vibrations of the C-O group appear at 1,082-1,072 cm^{-1} and 1,262-2,158 cm^{-1} . For Lov, the C=O stretching vibrations are found at 1,747 cm^{-1} . Meanwhile, for PLA, the band attributed to the stretching vibrations of C=O is shifted to a lower wavelength number range (1,722-1,696 cm^{-1}), and a valence vibration of -OH appears at 3,537 cm^{-1} along with characteristic bands of valence and deformation vibrations of =CH at 3,015 cm^{-1} and 966 cm^{-1} , respectively.

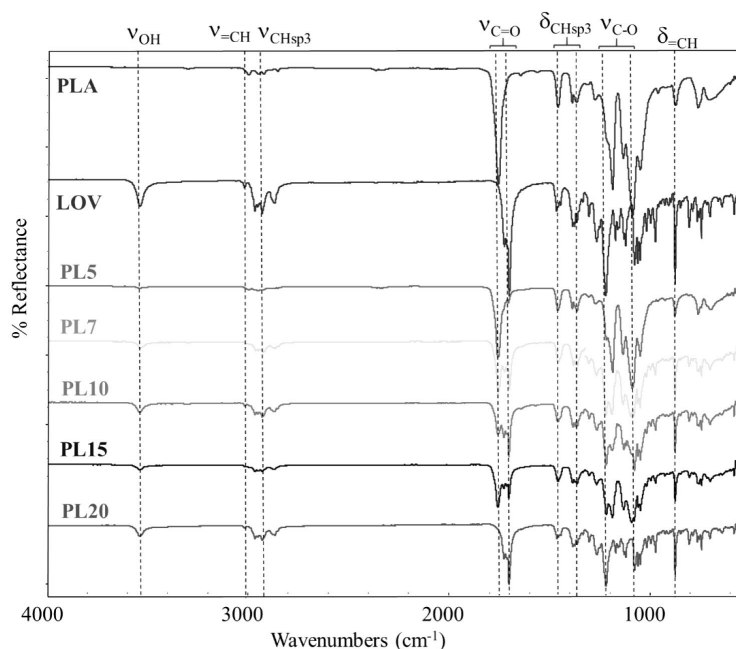


Figure 1. FT-IR spectra of PLA, Lov, and PLA/Lov biocomposites

Table 4: Characteristic FTIR spectral signals (cm⁻¹) of PLA/Lov biocomposites

Sample	ν_{OH}	$\nu_{CH\ sp^3}$	$\delta_{CH\ sp^3}$	$\nu_{=CH}$	$\delta_{=CH}$	$\nu_{C=O}$	ν_{C-O}
PLA	-	2994-2950	1452-1382	-	-	1747	1082; 1262
Lov	3537	2964-2865	1459-1355	3015	966	1722-1696	1072; 1258
PL5	3542	2994-2947	1455-1382	-	970	1754-1695	1083; 1265
PL7	3539	2963-2927	1456-1381	3015	968	1755-1697	1074; 1259
PL10	3538	2960-2927	1456-1369	3015	968	1754-1697	1074; 1260
PL15	3537	2961-2927	1455-1381	3018	968	1755-1697	1075; 1260
PL20	3537	2964-2927	1459-1380	3015	968	1722-1697	1072; 1260

In the FTIR spectra of the studied PLA/Lov materials, all characteristic bands of PLA and Lov are found, as shown in Figure 1 and Table 4. Notably, the valence vibration of the C=O group appears in two ranges, one at 1,955-1,954cm⁻¹ (corresponding to PLA) and the other at 1,722-1,695cm⁻¹ (corresponding to Lov). However, there are minor changes in the PLA/Lov biocomposites compared to the initial PLA and Lov, caused by the variation of the Lov ratio loaded in PLA. In these PLA/Lov biocomposites, there are Van der Waals interactions between molecules or hydrogen bonds between -OH and C=O groups. Therefore, physical interactions have formed between Lov and PLA molecules.

3.1.2. Morphology of PLA/Lov biocomposites

It can be seen from FESEM images of Lov and the PLA/Lov biocomposite samples in Figure 2 that Lov exists in rod-shaped crystals with a size of 15-20 nm. However,

when Lov was dispersed into the PLA polymer matrix, Lov particle size decreased to 200-650nm with a tendency to aggregate into clusters. Particles in PL samples have different sizes and tend to aggregate or return to their original rod shape depending on the dispersion ability and Lov ratio in the PLA matrix[30]. It was caused the formation of hydrogen bonds and weak interactions between molecules that form a spatial structure in the materials[31-32], as follows: When the low contents of Lov reduced the porosity of the structure; therefore, Lov particles were difficult to disperse into the polymer matrix. However, when too high contents of Lov were introduced into the material, it can cause steric hindrance, which limited the number of hydrogen bonds between Lov molecules and the PLA matrix, thereby decreasing the ability to disperse Lov particles into the PLA matrix, causing cluster aggregation of Lov particles[28, 31].

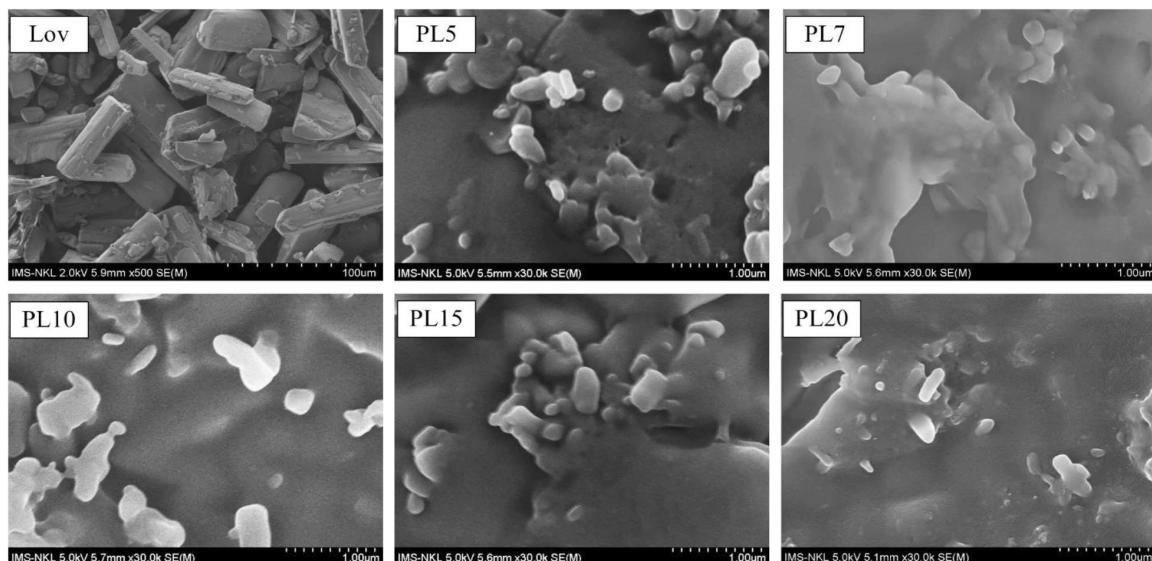


Figure 2. FESEM of Lov and PLA/Lov biocomposites

3.1.3. Thermal properties of PLA/Lov biocomposites

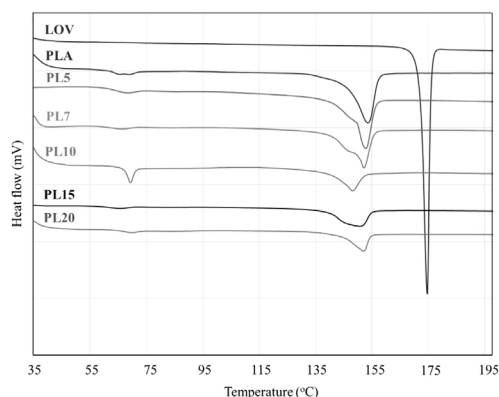


Figure 3. DSC diagrams of Lov, PLA, and PLA/Lov biocomposites

Table 5: DSC parameters obtained with Lov, LPA, and PLA/Lov biocomposites

Sample	First endothermic peak (°C)	Second endothermic peak (°C)
Lov	-	174.6
PLA	66.8 - 67.9	153.8
PL5	68.3	153.0
PL7	66.2	152.5
PL10	69.0	148.5
PL15	65.6	151.7
PL20	68.3	151.4

The DSC results presented in Figure 3 and Table 5 revealed that the single Lov sample has an endothermic peak corresponding to its melting point at 174.6°C and the

melting process occurs in the range of 172-177°C. This result is consistent with previous works and demonstrates the high purity of Lov[32-33]. Meanwhile, the DSC diagram of a single PLA shows two endothermic peaks, in which the second one corresponds to the melting at 153.8°C, consistent with the literature[34].

All PL samples exhibited two endothermic peaks in the ranges of 65.6-69.0°C and 148.5-153.0°C. However, the first endothermic peak can be attributed to the dehydration process of PLA and is too minor, only clearly observable in the sample PL10. This may be due to the uniform dispersion of Lov particles in the PLA matrix for the sample PL10, increasing its durability and reducing its dehydration ability.

When combining Lov and PLA in the composites, the melting point of the PLA/Lov materials is in the range of 148.5-153.0°C. This might be because when Lov was dispersed into the structure of the PLA polymer matrix, the size of Lov particles decreased, reducing the crystallinity, and thereby reducing the melting point of the composite compared to Lov[35]. Moreover, it can also be due to the formation of hydrogen bonds between Lov particles and the PLA matrix, leading to a lower particle size[34]. The sample PL10 has the lowest melting point (148.5°C), showing the uniform dispersion of Lov into the polymer matrix. This result is also consistent with the SEM result of the sample.

3.2. Lovastatin release from PLA/Lov biocomposites

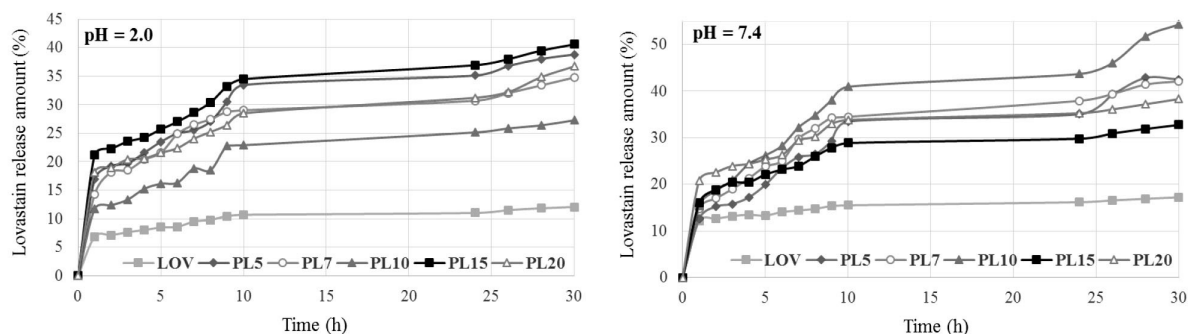


Figure 4. Time-dependent plots of Lov amounts released from PLA/Lov biocomposites in pH 2.0 (left) and pH 7.4 (right) buffers

The drug release testing results over time during 30 hours in the two buffer solutions are presented in Figure 4: in the simulated environment of lower gastric juice at pH 2.0 (on the left) and in the simulated environment of small intestinal fluid in the duodenal area at pH 7.4 (on the right). The release mechanism of Lov drug from PLA/Lov biocomposites consists of the penetration of water into the PLA polymer matrix and diffusion of the drug dispersed in the matrix due to swelling of the polymer.

It can be seen from Figure 4 that in pH 2.0 buffer, the Lov percentage released is in the range of 27.26-40.58%. Notably, the samples PL15 and PL5 exhibit the highest Lov release levels, of 21.19% and 18.18%, respectively, after 1 hour; 40.58%, and 38.80% after 30 hours. In contrast, sample PL10 had the lowest drug release level of 27.26% after 30 hours. Based on the results, the sample PL10 was found to have optimal drug release behavior because, with this sample, Lov could be better protected in gastric juice since its introduction.

In the pH 7.4 environment, Lov release preferentially occurs at a faster rate to ensure absorption of Lov into the bloodstream. This may be due to the swelling and the decomposition of PLA were faster in a pH 7.4 environment than in a pH 2.0 environment[28], thereby releasing Lov better. It can be seen that after 30 hours, the sample PL10 showed the most effective Lov release of 54.25% with the fastest rate, while the other samples only gave drug release levels in the range of 32.73-42.28%.

The investigation was also conducted with a control sample of a single Lov, and the results show that the Lov release level was 12.06% at pH 2.0 and 17.21% at pH 7.4. Based on the Lov drug release level, the optimal Lov: PLA ratio (1:10) was found in the sample PL10 because the Lov release was lower in pH 2.0 (gastric juice) and better in pH 7.4 (small intestinal fluid) with drug release levels of

27.26% và 54.25%, respectively, facilitating the absorption of Lov drug into the blood.

IV. CONCLUSION

The poly(lactic acid)/lovastatin biocomposites were fabricated with different mass ratios of Lov:PLA. The investigations of chemical structure, morphology, and thermal properties revealed that the Lov:PLA ratio of 1:10 (in the sample PL10) gave the optimal results with Lov particle size of 500-650nm and the best dispersion of Lov into the PLA matrix, which is consistent with DSC result showing a melting point of 148.5°C. In addition, the biocomposite with this Lov:PLA ratio also exhibited the most reasonable drug release properties in the environments simulating gastric juice (pH 2.0) and small intestinal fluid (pH 7.4). The obtained results are the basis for further research on the combination of lovastatin/poly(lactic acid) with other carrier materials to optimize the release ability and control the Lov drug release.

REFERENCES

- [1]. WHO Expert Committee on Specifications for Pharmaceutical Preparations N° 992, Annex 7 Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, 2015.
- [2]. Khadka P, Ro J, Kim H, Kim I, Kim JT, Kim H, et al, *Pharmaceutical particle technologies: An approach to improve drug solubility, dissolution and bioavailability*, Asian J. Pharm. Sci., 2014, 9, 304, 16.
- [3]. R. Ghadi, N. Dand, *BCS class IV drugs: Highly notorious candidates for formulation development*, J. Control Release., 2017, 248, 71-95.

- [4]. C. A. Lipinski, F. Lombardo, B. W. Dominy, P. J. Feeney, *Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings*, *Adv. Drug Deli. Review.*, 2012, 64(1-3), 4-17.
- [5]. C. Wu, J. Wang, Y. Hu, Z. Zhi, T. Jiang, J. Zhang, S. Wang, *Development of a novel starch-derived porous silica monolith for enhancing the dissolution rate of poorly water-soluble drug*, *Mat. Sci. Engineer.*, 2012, 32(2), 201-206.
- [6]. H. de Waard, et al, *Unexpected differences in dissolution behavior of tablets prepared from solid dispersions with a surfactant physically mixed or incorporated*, *Inter. J. Pharm.*, 2008, 349(1-2), 66-73.
- [7]. S. Kalepu, V. Nekkanti, *Insoluble drug delivery strategies: Review of recent advances and business prospects*, *Acta. Pharm. Sin. B.*, 2015, 5(5), 442-53.
- [8]. Umakant Verma, J.B. Naik, and V.J. Mokale, *American J. Pharm. Sci. Nanotech.*, 2014, 1(1), 11-26.
- [9]. D. V. Bhalani, B. Nutan, A. Kumar, and A. S. Chandel, *Bioavailability Enhancement Techniques for Poorly Aqueous Soluble Drugs and Therapeutics, Biomedicines.*, 2022, 10(9), 2055.
- [10]. T. P. Nguyen, T. C. Nguyen, Q. M. Vu, H. Thai, Q. T. Vu, *Some characteristics and allopurinol release of carrageenan/allopurinol films using polyethylene oxide as a dispersion aid agent*, *Vietnam J. Sci. Tech.*, 2020, 58(2), 219-227.
- [11]. Q. M. Vu, T. C. Nguyen, D. M. Ng. Dam, Q. T. Vu, T. L. Le, T. D. Hoang, T. K. N. Tran, T. A. Nguyen, P. H. Nguyen, H. Thai. *A novel method for preparation of carrageenan/fish scale collagen/ allopurinol biocomposite Film*, *Int. J. Polym. Sci.*, 2021, Article ID 9960233, 10 pages.
- [12]. T. M. Tran, T. C. Nguyen, Q. M. Vu, T. T. T. Nguyen, D. M. T. Tran, Q. T. Vu, V. H. Ha, H. Thai. *Effect of fish scale collagen on some characteristics and drug release of carrageenan/collagen/allopurinol film*, *Vietnam J. Sci. Tech.*, 2019, 57(3B), 1-8.
- [13]. Z. Dai, J. Deng, Q. Yu, R. M. L. Helberg, S. Janakiram, L. Ansaloni, and L. Deng, *Fabrication and evaluation of Bio-based nanocomposite TFC hollow fiber membranes for enhanced CO₂ Capture*, *ACS Appl. Mater. Interfaces.*, 2019, 11(11), 10874-10882.
- [14]. T. T. T. Nguyen, T. C. Nguyen, V. G. Nguyen, T. M. T. Dinh, D. L. Tran, H. Thai. *PLA/CS/Nifedipine nanocomposite films: Properties and the in-vitro release of nifedipine*, *J. Electron. Mater.*, 2016, 45(7), 3581-3590.
- [15]. C. Ok-Sun, J. Sung-Joo, S. Sang-Wan, P. Cheung-Seog, C. Jeong-Je, A. Hyun-Jong, *The 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor, lovastatin (statin) ameliorates CCK-induced acute pancreatitis in rats*, *Biol. Pharm. Bull.*, 2005, 28(8), 1394-1397.
- [16]. R. S. Cesare, *The pharmacology of statins*, *Pharm. Res.*, 2014, 88, 3-11.
- [17]. K. Sunghwan, C. Jie, C. Tiejun, G. Asta, H. Jia, H. Siqian, L. Qingliang, A. S. Benjamin, A. T. Paul, Y. Bo, Z. Leonid, Z. Jian, E. B. Evan, *PubChem 2019 update: Improved access to chemical data*, *Nucleic Acids Res.*, 2019, 47, D1102-D1109.
- [18]. S. Michael, *Chemical, pharmacokinetic and pharmacodynamic properties of statins: An update*, *Fundam Clin. Pharmacol.*, 2005, 19, 117-125.
- [19]. C.-C. Lucía, L.-C. José, *Cardiovascular Risk Factors in Pathology, Chapter: Pharmacokinetic Aspects of Statins*, 2020, Edited by Alaeddin Abukabda, Maria Suciú and Minodora Andor.
- [20]. G. F. Leisan, A. S. Holger, H. Daniel, A. Albert, K. Vladimir, *Interaction of statins with phospholipid bilayers studied by solid-state NMR spectroscopy*, *Biochim. Biophys. Acta Biomembr.*, 2019, 1861(3), 584-593.
- [21]. A. L. Kelly, G. Bruktawit, B. S. J. Evan, *Attenuation of experimental autoimmune neuritis with locally administered lovastatin encapsulating PLGA Nanoparticles*, *J. Neurochem.*, 2017, 140(2), 334-346.
- [22]. Z. Yazhe, M. Pyda, C. Peggy, *Electrospun fibers of poly(l-lactic acid) containing lovastatin with potential applications in drug delivery*, *J. Appl. Polym. Sci.*, 2017, 134(36), 45287.
- [23]. L. Gemma, C. Marco, P. Simone, L. Stefania, B. Claudia, T. Gabriella, D. Alessandro, R. Claudio, M. Agnese, *New formulations to enhance lovastatin release from red yeast rice (RYR)*, *J. Drug Deliv. Sci. Technol.*, 2016, 36, 110-119.
- [24]. N. Adelina-Gabriela, M. G. Alexandru, *Applications of chitosan-alginate-based nanoparticles-an up-to-date review*, *Nanomaterials*. 2022, 12(2), 186.

- [25]. T. D. M. Tran, C. T. Nguyen, T. Q. Do, G. L. Bach, N. H. Trinh, T. Q. Vu, H. Thai, *Preparation and characterization of chitosan/fish scale collagen/lovastatin nanocomposites*, J. Poly. Environ., 2020, 28(1), 2851-2863.
- [26]. H. Waled, B. Deon, chapter “Poly(lactic acid) as a biomaterial for cardiovascular devices and tissue engineering applications” in Book “Industrial Applications of Poly(lactic acid)”, Springer, 2017.
- [27]. G. Narayanan, V. N. Vernekar, E. L. Kuyinu, C. T. Laurencin, *Poly (lactic acid)-based biomaterials for orthopedic regenerative engineering*, Adv. Drug Deliv. Rev., 2016, 107, 247-276.
- [28]. T. Betty, G. David, M. Antonella, U. Tadanobu, B. Henry, *Polylactic acid (PLA) controlled delivery carriers for biomedical applications*, Adv. Drug Deliv. Rev., 2016, 107, 163-175.
- [29]. C. T. Nguyen, T. T. T. Nguyen, T. M. T. Dinh, H. X. T. To, G. V. Nguyen, Q. M. Pham, D. T. Nguyen, H. Thai, *Thermal property, morphology, and hydrolysis ability of poly(lactic acid)/chitosan nanocomposites using polyethylene oxid*, J. Appl. Polym. Sci., 2015.
- [30]. H. Thai, C. T. Nguyen, L. T. Thach, M. T. Tran, H. D. Mai, T. T. T. Nguyen, G. D. Le, M. V. Can, L. D. Tran, G. L. Bach, K. Ramadass, C. I. Sathish, Q. V. Le, *Characterization of chitosan/alginate/lovastatin nanoparticles and investigation of their toxic effects in vitro and in vivo*, Scientific Reports, 2020, 10(1), 909.
- [31]. H. M. Ha, M. Q. Vu, T. T. T. Vu, T. P. T. Doan, D. T. Pham, V. T. B. Nguyen, L. K. Duong, L. N. Nguyen, Y. O. T. Doan, C. T. Nguyen, H. Thai, T. Q. Vu, *Evaluation of the effect of the chitosan/carrageenan ratio on lovastatin release from chitosan/carrageenan based biomaterials*, Vietnam J. Chem., 2022, 60, 72-79.
- [32]. T. T. T. Vu, N. T. H. Nguyen, M. Q. Vu, L. N. Nguyen, V. T. B. Nguyen, T. Q. Vu, *Synthesis and characterization of chitosan/carrageenan/polyaniline-based biocomposite as lovastatin carrier and its drug release ability in buffer solutions*, HNUE Journal of Science, Nat. Sci., 2023, 68(3), 64-74.
- [33]. V. Radhika, N. Manju, T. G. Singh, S. Manjinder, A. Geeta, *Improved Efficacy of Lovastatin from Soluplus-PEG Hybrid Polymer- Based Binary Dispersions*, Current Bioactive Comp., 2020, 16(8), 1164-1171.
- [34]. D. Battagazzore, S. Bocchini, A. Frache, *Crystallization kinetics of poly(lactic acid)-talc composites*, Express Polym. Lett., 2011, 5(10), 849-858.
- [35]. I. M. Minisy, N. A. Salahuddin, M. M. Ayad, *In vitro release study of ketoprofen loaded chitosan/polyaniline nanofibers*, Poly. Bull., 2021, 78, 5609-5622. ❖