

**LÝ LỊCH KHOA HỌC**

*(Theo mẫu tại Thông tư số 08/2011/TT-BGDĐT ngày 17/02/2011 của Bộ trưởng Bộ GDĐT – Phụ lục V)*

**I. LÝ LỊCH SƠ LƯỢC**

Họ và tên: TRẦN THỊ PHƯỢNG      Giới tính: Nữ  
Ngày, tháng, năm sinh: 24/02/1988      Nơi sinh: Đồng Kỳ - Yên Thế - Bắc Giang  
Quê quán: Đồng Kỳ - Yên Thế - Bắc Giang      Dân tộc: Kinh  
Học vị cao nhất: Tiến sỹ      Năm, nước nhận học vị: 2018  
Chức danh khoa học cao nhất: ..... Năm bổ nhiệm: .....  
Chức vụ (hiện tại hoặc trước khi nghỉ hưu): .....  
Đơn vị công tác (hiện tại hoặc trước khi nghỉ hưu): .....  
Chỗ ở riêng hoặc địa chỉ liên lạc: Khu Ba Góc – Tổ dân phố Đồng Quán – Thị Trấn Bó  
Hạ – Yên Thế – Bắc Giang  
Điện thoại liên hệ: CQ: .....NR: .....DD: 0866.653.197  
Fax: ..... E-mail: phuongtran24288@gmail.com  
Số CMND: 121848730 Ngày cấp: 21/11/2005 Nơi cấp: Đồng Kỳ - Yên Thế - Bắc Giang

**II. QUÁ TRÌNH ĐÀO TẠO**

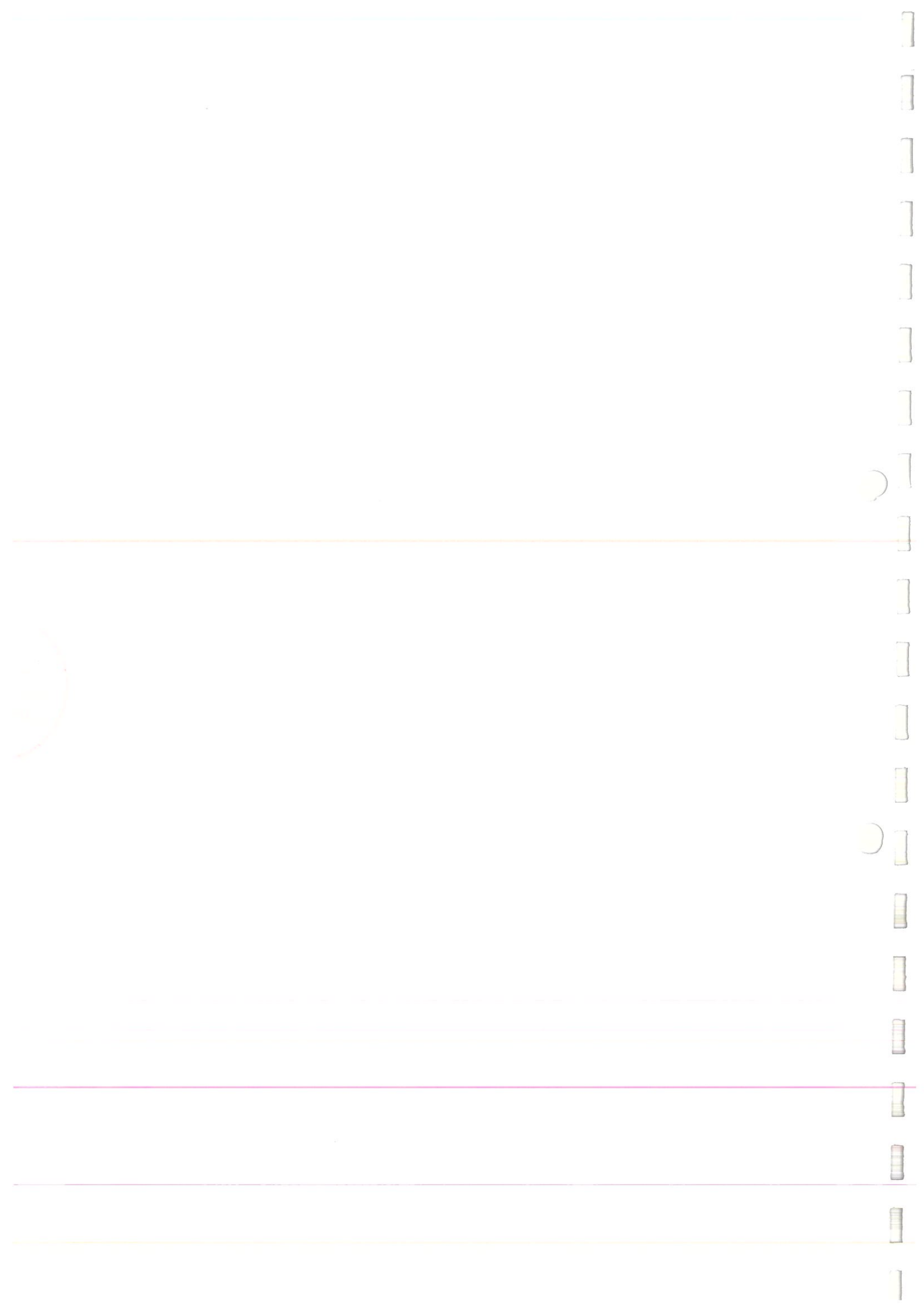
**1. Đại học:**

Hệ đào tạo: Chính quy .....  
Nơi đào tạo: Đại học Y Dược Thái Nguyên .....  
Ngành học: Dược .....  
.....  
Nước đào tạo: Việt Nam ..... Năm tốt nghiệp: 2011 .....  
Bằng đại học 2: ..... Năm tốt nghiệp: .....

**2. Sau đại học**

- Thạc sỹ chuyên ngành: Dược ..... Năm cấp bằng: 2014.....  
Nơi đào tạo: Đại học quốc gia Chonnam, Hàn Quốc .....
- Tiến sỹ chuyên ngành: Dược..... Năm cấp bằng: 2018.....  
Nơi đào tạo: Đại học quốc gia Chonnam, Hàn Quốc .....
- Tên luận án:  
Thạc sỹ: Enhanced bioavailability and lymphatic delivery of paclitaxel by using lipid nanocapsules (Tăng cường sinh khả dụng và vận chuyển paclitaxel vào bạch huyết bằng cách sử dụng hệ nano lipid)







Tiến sỹ: The role of CYP3A5 and MDR1 genetic polymorphisms in population pharmacokinetics of felodipine in healthy Korean subjects (Vai trò của đa hình di truyền CYP3A5 và MDR1 trong dược động học quần thể của felodipin ở người Hàn Quốc khỏe mạnh)

- 3. Ngoại ngữ:**
1. Tiếng hàn TOPIK 4..... Mức độ sử dụng: Tốt.....
  2. .... Mức độ sử dụng: .....
  3. .... Mức độ sử dụng: .....

### III. QUÁ TRÌNH CÔNG TÁC CHUYÊN MÔN

Thời gian	Nơi công tác	Công việc đảm nhiệm
11/2018-05/2022	Khoa dược trường đại học quốc gia Chungnam, Hàn Quốc	Nghiên cứu sau tiến sỹ
08/2022-09/2023	Khoa y học phương đông trường đại học KyungHee, Hàn Quốc	Nghiên cứu sau tiến sỹ
12/2023-Nay	Học viện Y Dược học cổ truyền Việt Nam	Giảng Viên

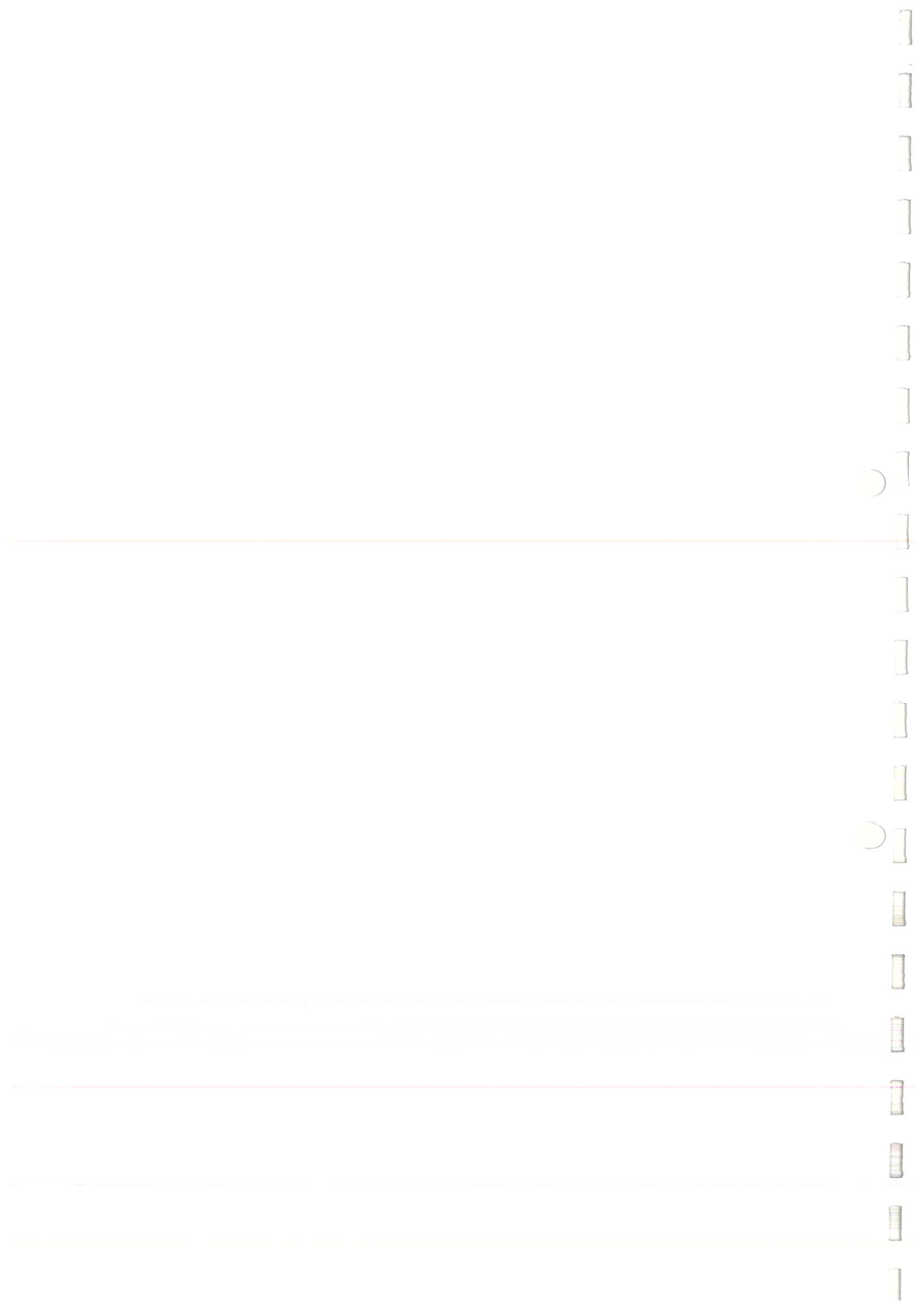
### IV. QUÁ TRÌNH NGHIÊN CỨU KHOA HỌC

1. Các đề tài nghiên cứu khoa học đã và đang tham gia:

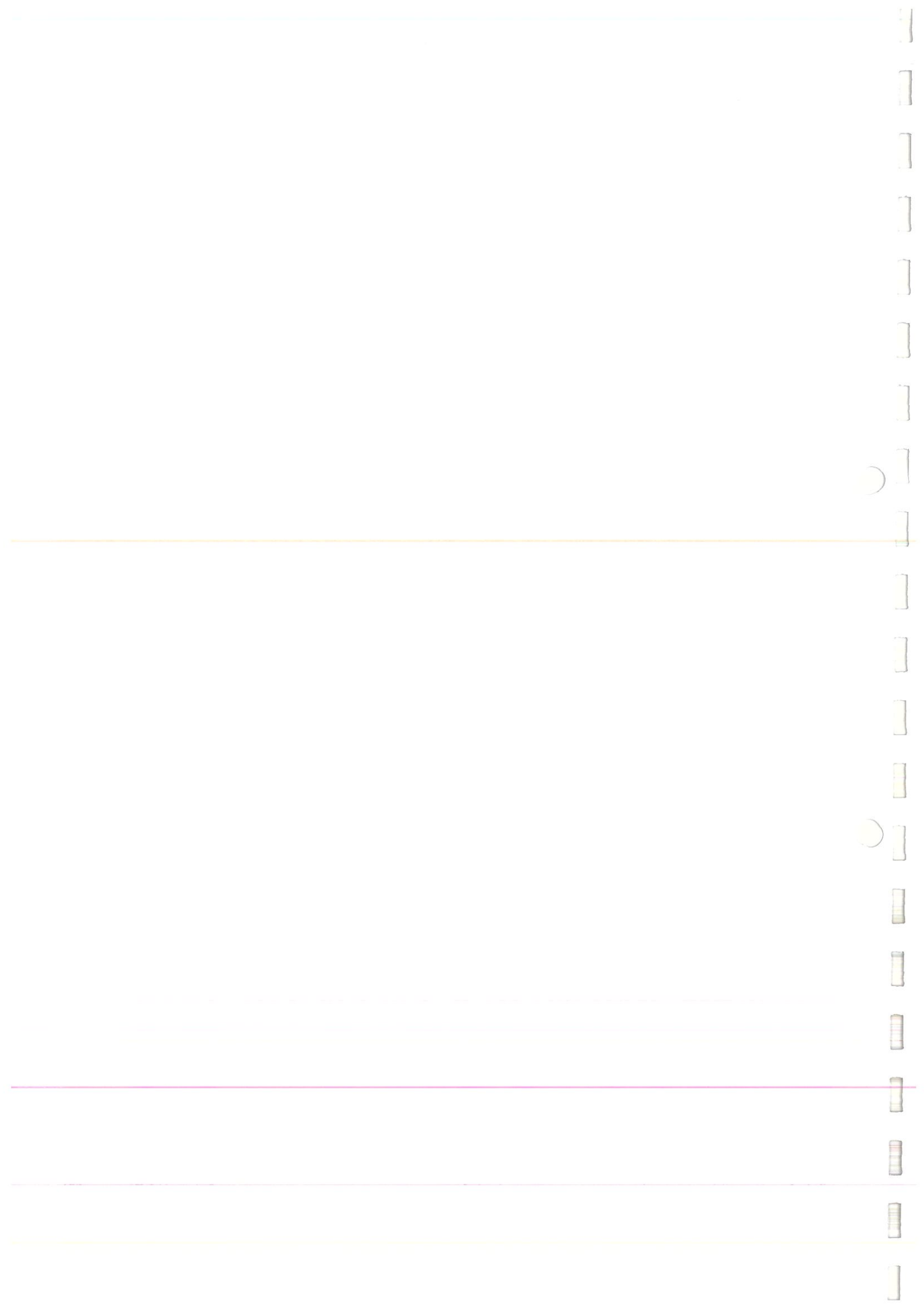
TT	Tên đề tài nghiên cứu	Năm bắt đầu/Năm hoàn thành	Đề tài cấp (NN, Bộ, ngành, trường)	Trách nhiệm tham gia trong đề tài

2. Các công trình khoa học đã công bố:

TT	Tên công trình	Năm công bố	Tên tạp chí
1	Tổng quan: Liệu pháp điều trị ung thư của phức hợp alpha-lactalbumin và acid oleic	2024	Tạp chí Dược liệu
2	Nghiên cứu bào chế hệ nano lipid rắn chứa celecoxib và đánh giá khả năng ức chế một số dòng tế bào ung thư vú in vitro	2024	Tạp chí Y Dược học quân sự
3	Sialic acid-decorated liposomes	2023	Biomaterials Advances

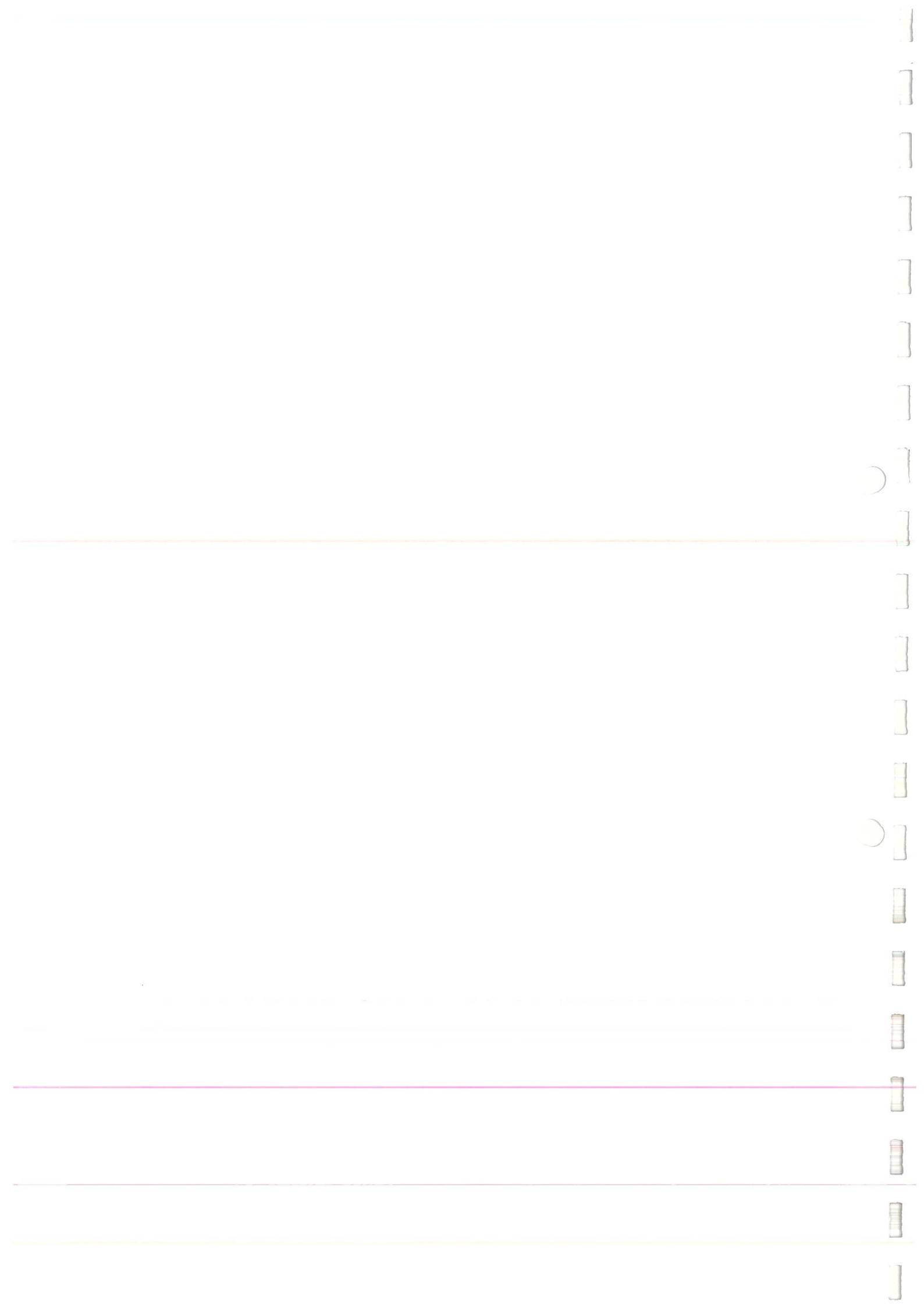


	<p>enhance the anti-cancer efficacy of docetaxel in tumor-associated macrophages</p> <p>Các liposome được trang trí bằng axit sialic tăng cường hiệu quả chống ung thư của docetaxel trong các đại thực bào liên quan đến khối u</p>		
4	<p>Solid dispersion of mebendazole via surfactant carrier to improve oral bioavailability and in vitro anticancer efficacy</p> <p>Phân tán rắn mebendazole qua chất mang hoạt tính bề mặt để cải thiện sinh khả dụng đường uống và hiệu quả chống ung thư trong ống nghiệm</p>	2023	Journal of Pharmaceutical Investigation
5	<p>Cinnamomum cassia and Rosa laevigata mixture improves benign prostatic hyperplasia in rats by regulating androgen receptor signaling and apoptosis</p> <p>Hỗn hợp Cinnamomum cassia và Rosa laevigata cải thiện chứng tăng sản tuyến tiền liệt lành tính ở chuột bằng cách điều chỉnh tín hiệu thụ thể androgen và apoptosis</p>	2023	Nutrients
6	<p>Co-carrier-based solid dispersion of celecoxib improves dissolution rate and oral bioavailability in rats</p> <p>Hệ phân tán rắn dựa trên chất mang đồng thời của celecoxib cải thiện tốc độ hòa tan và sinh khả dụng đường uống ở chuột</p>	2022	Journal of Drug Delivery Science and Technology
7	<p>Alginate-coated chitosan nanoparticles protect protein drugs from acid degradation in gastric media</p> <p>Các hạt nano chitosan được phủ alginate bảo vệ thuốc protein khỏi sự</p>	2022	Journal of Pharmaceutical Investigation

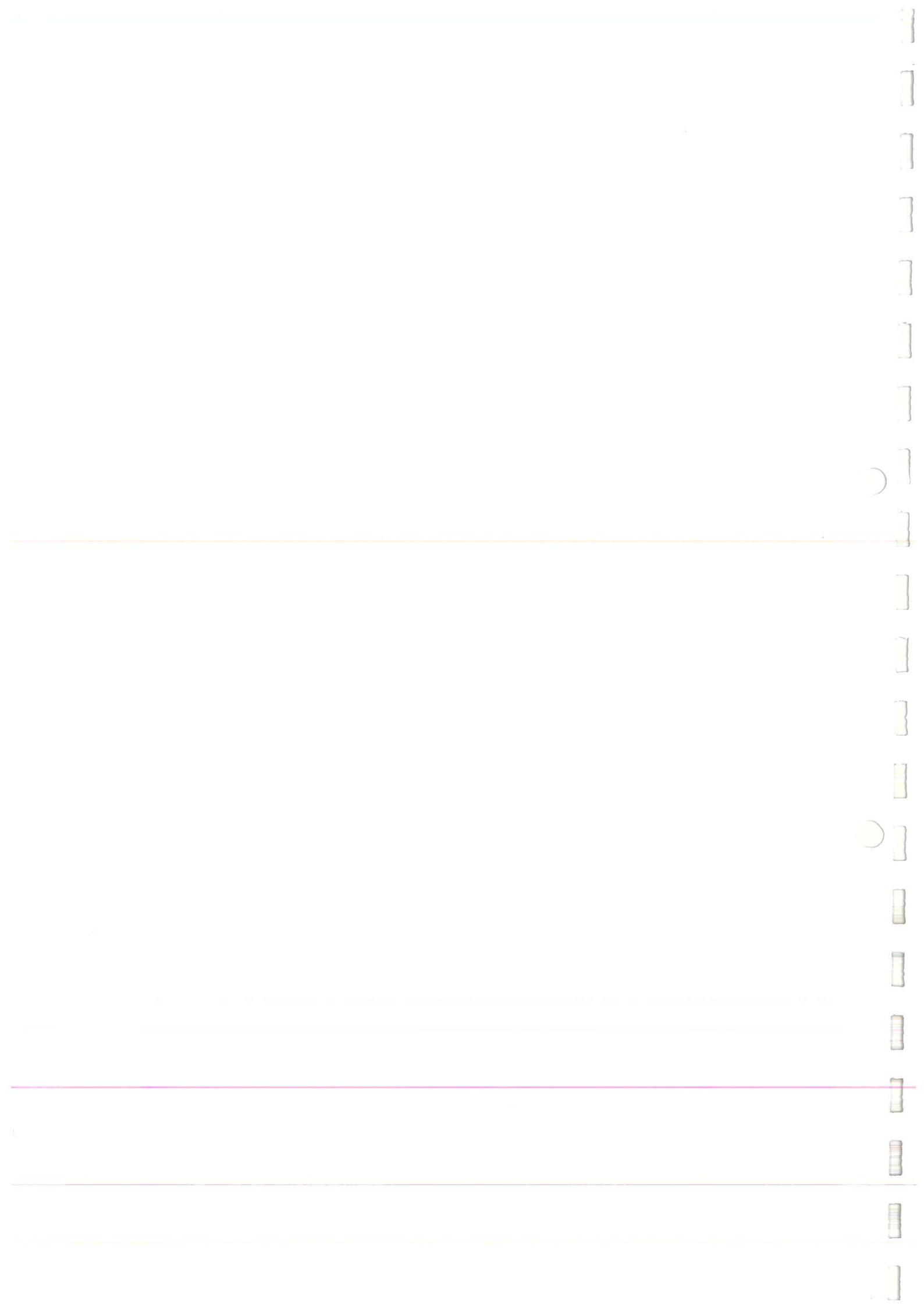


	phân hủy axit trong dịch vị dạ dày		
8	<p>Application of supercritical fluid technology for solid dispersion to enhance solubility and bioavailability of poorly water-soluble drugs</p> <p>Ứng dụng công nghệ chất lỏng siêu tới hạn để phân tán rắn nhằm tăng cường độ hòa tan và sinh khả dụng của thuốc kém tan trong nước</p>	2021	International Journal of Pharmaceutics
9	<p>Oral and lymphatic delivery of paclitaxel via lipid nanocapsules</p> <p>Vận chuyển paclitaxel qua đường uống và bạch huyết thông qua hệ thống nano lipid</p>	2021	Yakhak Hoeji
10	<p>Local drug delivery using poly(lactic-co-glycolic acid) nanoparticles in thermosensitive gels for inner ear disease treatment</p> <p>Phân phối thuốc tại chỗ bằng cách sử dụng hạt nano poly(lactic-co-glycolic acid) trong gel nhạy nhiệt để điều trị bệnh tai trong</p>	2021	Drug Delivery
11	<p>Docetaxel-loaded PLGA nanoparticles to increase pharmacological sensitivity in MDA-MB-231 and MCF-7 breast cancer cell</p> <p>Các hạt nano PLGA được nạp docetaxel để tăng độ nhạy dược lý trong tế bào ung thư vú MDA-MB-231 và MCF-7</p>	2021	The Korean Journal of Physiology & Pharmacology
12	<p>Formulation of solid dispersion to improve dissolution and oral bioavailability of poorly soluble dexibuprofen</p> <p>Xây dựng hệ phân tán rắn để cải thiện độ hòa tan và sinh khả dụng đường uống của dexibuprofen kém hòa tan</p>	2021	Pharmaceutical Development and Technology

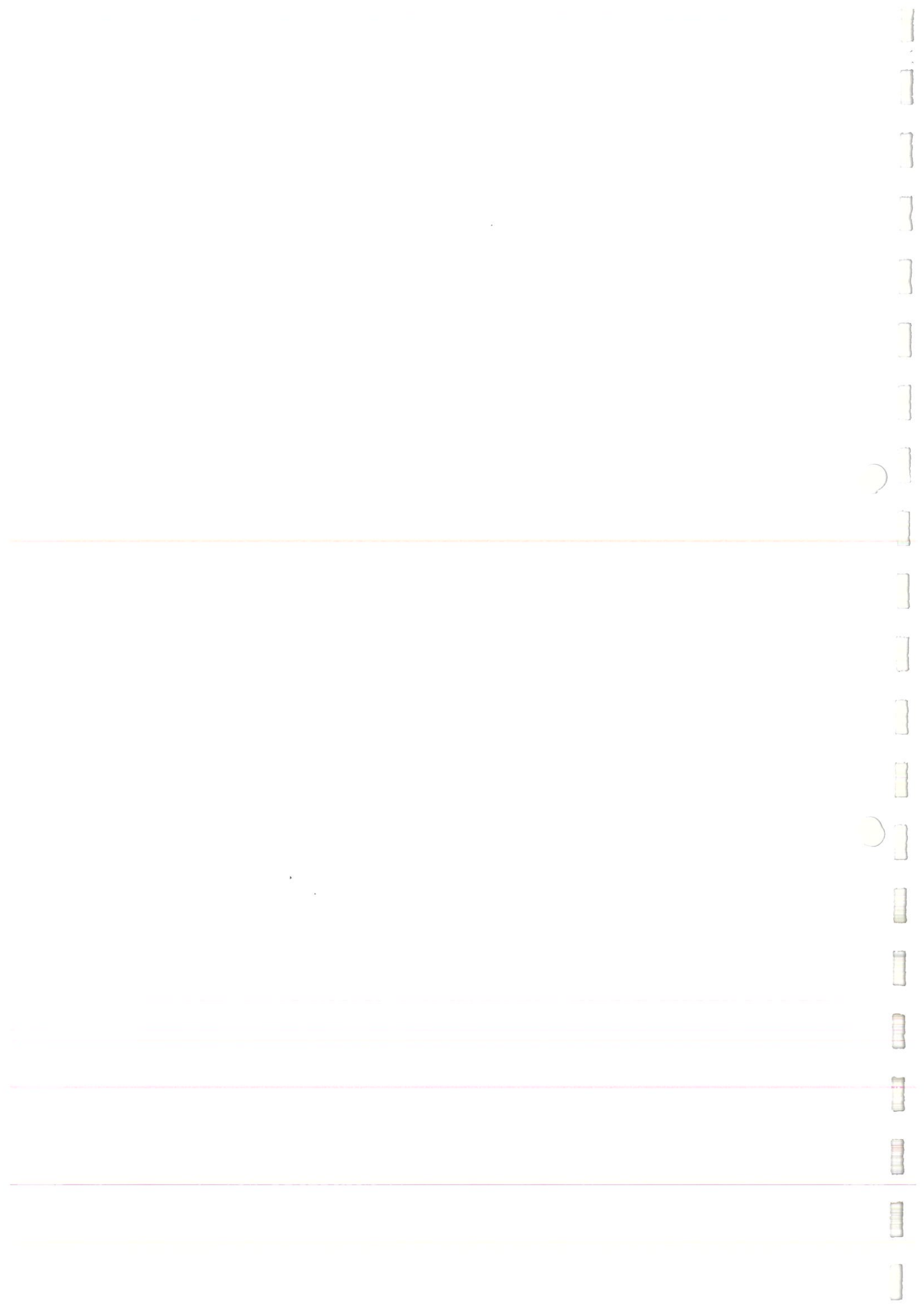




13	<p>Recent trends of self-emulsifying drug delivery system for enhancing the oral bioavailability of poorly water-soluble drugs</p> <p>Xu hướng gần đây về hệ thống phân phối thuốc tự nhũ hóa nhằm tăng cường sinh khả dụng đường uống của các thuốc ít tan trong nước</p>	2021	Journal of Pharmaceutical Investigation
14	<p>Chitosan-coated nanostructured lipid carriers of fenofibrate with enhanced oral bioavailability and efficacy</p> <p>Chất mang lipid cấu trúc nano được phủ chitosan của fenofibrate giúp tăng cường sinh khả dụng và hiệu quả qua đường uống</p>	2020	Colloids and Surfaces B: Biointerfaces
15	<p>Effect of calcium chloride on the protein encapsulation and stability of proliposomal granules</p> <p>Ảnh hưởng của canxi clorua đến quá trình đóng gói protein và tính ổn định của hạt proliposome</p>	2020	Journal of Drug Delivery Science and Technology
16	<p>Recent advances of nanotechnology for the delivery of anticancer drugs for breast cancer treatment</p> <p>Những tiến bộ gần đây của công nghệ nano trong việc cung cấp thuốc chống ung thư để điều trị ung thư vú</p>	2019	Journal of Pharmaceutical Investigation
17	<p>Solubility enhancement and application of cyclodextrins in local drug delivery</p> <p>Tăng cường độ hòa tan và ứng dụng cyclodextrin trong phân phối thuốc tại chỗ</p>	2019	Journal of Pharmaceutical Investigation
18	<p>Overview of the manufacturing methods of solid dispersion technology for improving the solubility of poorly water-soluble drugs and application to anticancer drugs</p>	2019	Pharmaceutics

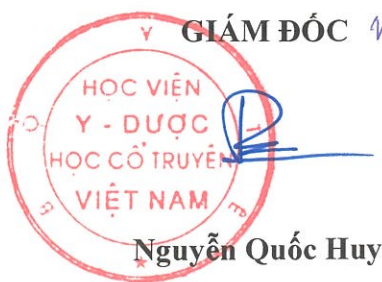


	Tổng quan các phương pháp sản xuất hệ phân tán rắn nhằm nâng cao độ hòa tan của thuốc kém tan trong nước và ứng dụng vào thuốc chống ung thư		
19	Population pharmacokinetics of gabapentin in healthy Korean subjects with influence of genetic polymorphisms of ABCB1  Dược động học quần thể của gabapentin ở đối tượng khỏe mạnh Hàn Quốc có ảnh hưởng đến đa hình di truyền của ABCB1	2017	Journal of Pharmacokinetics and Pharmacodynamics
20	Population pharmacokinetic analysis of rebamipide in healthy Korean subjects with the characterization of atypical complex absorption kinetics  Phân tích dược động học quần thể của rebamipide ở các đối tượng khỏe mạnh ở Hàn Quốc với đặc điểm động học hấp thu phức tạp không điển hình	2017	Journal of Pharmacokinetics and Pharmacodynamics
21	Simultaneous determination of imperatorin and its metabolite xanthotoxol in rat plasma and urine by LC-MS/MS and its application to pharmacokinetic studies  Xác định đồng thời imperatorin và chất chuyển hóa xanthotoxol trong huyết tương chuột và nước tiểu bằng LC-MS/MS và ứng dụng của nó vào nghiên cứu dược động học	2017	Journal of Chromatography B
22	Preparation and evaluation of solid-self-emulsifying drug delivery system containing paclitaxel for lymphatic delivery  Nghiên cứu và đánh giá hệ thống phân phối thuốc tự nhũ hóa rắn chứa paclitaxel để phân phối thuốc vào bạch	2016	Journal of Nanomaterial





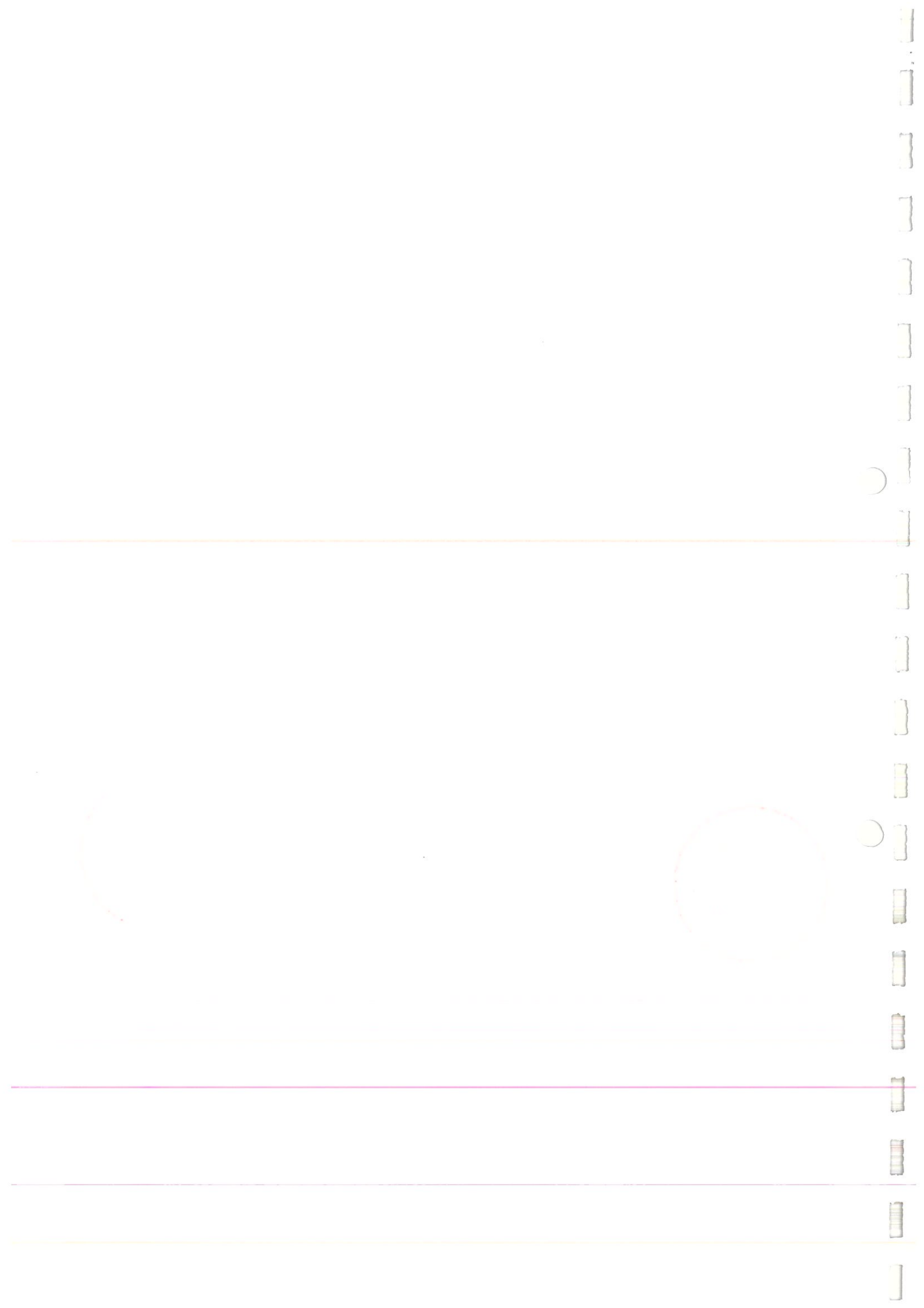
	huyết		
23	<p>Palbinone from <i>Paeonia suffruticosa</i> protects hepatic cells via up-regulation of heme oxygenase-1</p> <p>Palbinone từ <i>Paeonia suffruticosa</i> bảo vệ tế bào gan thông qua việc điều chỉnh tăng heme oxyase-1</p>	2014	Phytotherapy Research
24	<p>Chemical components from the fruit peels of <i>Wisteria floribunda</i> and their effects on rat aortic vascular smooth muscle cells</p> <p>Thành phần hóa học từ vỏ quả <i>Wisteria floribunda</i> và tác dụng của chúng đối với tế bào cơ trơn mạch máu động mạch chủ chuột</p>	2011	Bulletin of the Korean Chemical Society
25	<p>Adlay seed extract (<i>Coix lachryma-jobi</i> L.) decreased adipocyte differentiation and increased glucose uptake in 3T3-L1 cells</p> <p>Chiết xuất hạt Adlay (<i>Coix lachryma-jobi</i> L.) làm giảm sự biệt hóa tế bào mỡ và tăng sự hấp thu glucose ở tế bào 3T3-L1</p>	2010	Journal of Medicinal Food



Hà Nội, ngày 6 tháng 6 năm 2024

**Người khai ký tên**

**Trần Thị Phụng**



BẢN DỊCH

TRƯỜNG ĐẠI HỌC QUỐC GIA CHONNAM

BẢN SAO

Theo đề nghị của Khoa và được phép của pháp luật  
TRƯỜNG ĐẠI HỌC QUỐC GIA CHONNAM cấp cho

TRẦN THỊ PHƯỢNG

**BẰNG TIẾN SĨ**

**CHUYÊN NGÀNH DƯỢC**

Được hưởng mọi quyền lợi, danh dự, đặc quyền cũng như nghĩa vụ và trách nhiệm khác  
Cấp ngày 24 tháng 8 năm 2018

KHOA SAU ĐẠI HỌC  
TRƯỞNG KHOA  
(Đã ký)

TRƯỜNG ĐẠI HỌC QUỐC GIA CHONNAM  
Hiệu trưởng  
(đã ký, đóng dấu)



01278



Tôi là Nguyễn Quang Năng, CMND số 121308357, do CA Bắc Giang cấp ngày 15/4/2015, cam đoan dịch chính xác văn bản này từ tiếng Anh sang tiếng Việt  
Bắc Giang, Ngày 14 tháng 10 năm 2019  
Người dịch



Nguyễn Quang Năng

Ngày 14 tháng 10 năm 2019 (Ngày mười bốn, tháng mười, năm hai nghìn mười chín)  
Tại Phòng tư pháp huyện Lạng Giang, tỉnh Bắc Giang.

Tôi: Nguyễn Việt Anh

Là phó trưởng phòng tư pháp  
Chứng thực ông: Nguyễn Quang Năng là người đã ký vào bản dịch này trước mặt tôi.

Số chứng thực: ...6.76...

Quyển số: .....0.1.../SCT/CKND

Ngày 14 tháng 10 năm 2019

**CHỨNG THỰC**  
**BẢN SAO ĐÚNG VỚI BẢN CHÍNH**  
Ngày 28-02-2024  
Số CT: 388 ..... Q.số: 01 ..... SCT-BS



**PHÓ TRƯỞNG PHÒNG**  
**NGUYỄN VIỆT ANH**



**PHÓ CHỦ TỊCH**  
**NGUYỄN ĐOÀN KHÔI**





PHÓ CHỦ TỊCH  
NGUYỄN ĐOÀN KHÔI



PHÓ CHỦ TỊCH  
NGUYỄN ĐOÀN KHÔI



**BẢN SAO**

# GIẤY CÔNG NHẬN

## CỤC TRƯỞNG CỤC QUẢN LÝ CHẤT LƯỢNG

### CÔNG NHẬN

Văn bằng của Trường Đại học Quốc gia Chonnam, Hàn Quốc

Số hiệu: ; cấp ngày 24 tháng 8 năm 2018 cho:

Bà Trần Thị Phương

Sinh ngày 24 tháng 02 năm 1988

Là văn bằng: Tiến sĩ

Ngành/chuyên ngành đào tạo: Dược

Thời gian đào tạo: 4.5 năm

Hình thức đào tạo: Trực tiếp tại Hàn Quốc

Nhận xét: Trình độ đào tạo tương đương Bậc 8 trong Khung trình độ quốc gia Việt Nam.

**CHỨNG THỰC**  
**BẢN SAO ĐÚNG VỚI BẢN CHÍNH**

Ngày 15-12-2023

Số CT: 3076 Q.số: 02 SCT-BS

Hà Nội, ngày 12 tháng 12 năm 2023



**CỤC TRƯỞNG**

Huỳnh Văn Chương



PHỖ CHỦ NHIỆM  
TANG THỊ NGOẠN



Số vào sổ cấp giấy công nhận: 05193/2023/TS

Địa chỉ cổng thông tin điện tử truy cập để kiểm tra: <https://naric.edu.vn/front/tra-cuu-van-bang>

RYN 240

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# Chonnam National University

On the nomination of the faculty and as authorized by law,  
Chonnam National University has conferred on

**THI PHUONG TRAN**

the degree of

**Doctor of Philosophy in Pharmacy**

together with all the honors, rights, privileges and responsibilities pertaining thereto

Presented this August 24, 2018

*Cha Seong Sig*

Dean, The Graduate school

*Byungseok Jeong*

President

OFFICIAL SEAL  
OF THE UNIVERSITY








# 한국어능력시험 성적증명서

## OFFICIAL TOPIK SCORE REPORT

### 수험자 정보 (Test-taker's Information)

	성명 Name	성별 Gender	응시국가 Country	생년월일 Date of Birth
	TRAN THI PHUONG	여자(female) F	대한민국 KOREA	1988/02/24 yyyy/mm/dd
	수험번호 Registration No.	시험종류 Test Type	회차/시험일 Test Held/Test Date	성적유효기간 Valid Until
	001018000442	TOPIK II	88/2023/05/14 th/yyyy/mm/dd	2025/06/21 yyyy/mm/dd

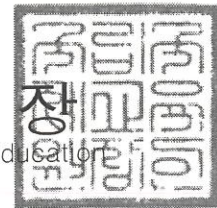
### 시험 결과 (Test Result)

영역 Section	점수 Score	수험자점수 및 수험집단평균 your score average	총점 TotalScore	등급 Level
듣기 Listening	62 / 100	62 / 59.68	163 / 300	4급
쓰기 Writing	43 / 100	43 / 38.59		
읽기 Reading	58 / 100	58 / 55.79		

### 언어 수행 능력 (Level Description)

시험종류 Test Type	TOPIK II	등급 Level	4급
듣기 Listening	사회적 관계 유지에 필요한 친숙하고 일반적인 사회적, 추상적 소재를 다룬 대화나 담화, 그리고 비교적 평이한 내용을 다룬 뉴스나 토론을 듣고 내용을 파악하고 추론할 수 있다.		
쓰기 Writing	사회적인 맥락과 관련된 일반적이거나 친숙한 사회적 소재의 설명문 또는 감상문을 단락 단위로 정확하고 적절하게 구성할 수 있다.		
읽기 Reading	사회생활에 필요한 글, 경제, 문화 분야의 소재를 다룬 글을 읽고 내용을 이해하고 추론할 수 있다. 감상문, 사용설명서, 안내문, 설명문, 신문 기사, 수필 등을 읽고 정보를 파악하며 내용을 추론할 수 있다.		

국립국제교육원  
President of National Institute for International Education







CỘNG HÒA XÃ HỘI CHỦ NGHĨA VIỆT NAM  
Độc lập - Tự do - Hạnh phúc

## CHỨNG CHỈ

### BỒI DƯỠNG NGHIỆP VỤ SƯ PHẠM

Cấp cho: **Trần Thị Phượng**  
Sinh ngày: **24/02/1988** Nơi sinh: **Bắc Giang**

Đã hoàn thành chương trình

Bồi dưỡng nghiệp vụ sư phạm cho giảng viên đại học, cao đẳng

Từ ngày **07** tháng **12** năm **2023** đến ngày **21** tháng **01** năm **2024**

Hội đồng thi: **Học viện Quản lý giáo dục**

Xếp loại: **Khá**

*Hà Nội*, Ngày **28** tháng **02** năm **2024**

HỌC VIỆN QUẢN LÝ GIÁO DỤC  
KT. GIÁM ĐỐC  
PHÓ GIÁM ĐỐC

Số hiệu: **011000**

Số vào sổ cấp chứng chỉ: **794**

*Phượng*  
TS. Phan Hồng Dương

**CHỨNG THỰC BẢN SAO ĐÚNG VỚI BẢN CHÍNH**  
Số chứng thực..... quyển số ..... - SCT/BS

Ngày: **15-05-2024**

**TU. CHỦ TỊCH**  
**CÔNG CHỨC TƯ PHÁP - HỘ TỊCH**



*Nguyễn Thị Việt Hà*





BỘ Y TẾ  
HỌC VIỆN YDHCT VIỆT NAM

CỘNG HÒA XÃ HỘI CHỦ NGHĨA VIỆT NAM  
Độc lập - Tự do - Hạnh phúc

Số: 25 /HDLĐ

Hà Nội, ngày 28 tháng 11 năm 2024

**HỢP ĐỒNG LAO ĐỘNG**  
**THỰC HIỆN CÔNG VIỆC CHUYÊN MÔN, NGHIỆP VỤ**

Căn cứ Bộ luật Lao động ngày 20 tháng 11 năm 2019;

Căn cứ Nghị định số 111/2022/NĐ-CP ngày 30 tháng 12 năm 2022 của Chính phủ về hợp đồng đối với một số loại công việc trong cơ quan hành chính và đơn vị sự nghiệp công lập;

Căn cứ nhu cầu và khả năng thực tế của các bên trong hợp đồng;

Hôm nay, ngày 28 tháng 11 năm 2024 tại Học viện Y-Dược học cổ truyền Việt Nam, chúng tôi gồm các bên dưới đây:

**BÊN A: NGƯỜI SỬ DỤNG LAO ĐỘNG**

Cơ quan, đơn vị: Học viện Y - Dược học cổ truyền Việt Nam

Địa chỉ: Số 2 Trần Phú, Hà Đông, Hà Nội

Điện thoại: 024.33824930

Số tài khoản: 3716.1.1057117

Mở tại: Kho bạc Nhà nước Hà Đông

Mã ĐVQHNS: 1057117

Đại diện theo pháp luật: Ông Nguyễn Quốc Huy

Chức vụ: Giám đốc Học viện

**BÊN B: NGƯỜI LAO ĐỘNG**

**Bà Trần Thị Phượng**

Sinh ngày 24 tháng 02 năm 1988 tại Bắc Giang

Giới tính: Nữ

Địa chỉ nơi cư trú: TDP Đồng Quán, Thị trấn Bồ Hạ, Yên Thế, tỉnh Bắc Giang

Điện thoại: 0866653197

Mã số thuế (nếu có):

Tài khoản ngân hàng: 100880553391

Nơi mở tài khoản: Ngân hàng Vietinbank

Email (nếu có): phuongtran24288@gmail.com

Số CMND/CCCD/Hộ chiếu: 024188017586

Cấp ngày: 10 tháng 11 năm 2023

Tại: Cục Cảnh sát QLHC về TTXH



Trình độ chuyên môn: Tiến sĩ chuyên ngành dược

Chuyên ngành đào tạo: Dược

Trình độ tin học:

Trình độ ngoại ngữ: Tiếng Hàn TOPIK 4

Hai bên thỏa thuận ký kết hợp đồng lao động và cam kết thực hiện những nội dung sau đây:

## **Điều 1. Công việc, vị trí việc làm và thời hạn hợp đồng**

### **1. Thời hạn hợp đồng**

Bên A và bên B thỏa thuận ký kết hợp đồng xác định thời hạn, cụ thể như sau:

Thời hạn của hợp đồng lao động: 12 tháng, kể từ ngày 01 tháng 12 năm 2024 đến ngày 30 tháng 11 năm 2025.

Trong thời hạn 30 ngày kể từ ngày hợp đồng lao động này hết hạn, bên A và bên B phải thỏa thuận để ký kết hợp đồng lao động mới; trong thời gian chưa ký kết hợp đồng lao động mới thì quyền, nghĩa vụ và lợi ích của hai bên được thực hiện theo hợp đồng này.

Trường hợp bên A và bên B tiếp tục thỏa thuận ký kết hợp đồng lao động mới là hợp đồng xác định thời hạn thì chỉ được ký thêm 01 lần. Hết thời hạn ký kết hợp đồng lần thứ 2, nếu bên B vẫn tiếp tục làm việc thì phải ký kết hợp đồng lao động không xác định thời hạn.

Trường hợp hết thời hạn 30 ngày kể từ ngày hợp đồng lao động này hết hạn mà bên A và bên B không ký kết hợp đồng lao động mới và không có thỏa thuận khác thì hợp đồng này đương nhiên trở thành hợp đồng lao động không xác định thời hạn.

### **2. Công việc và vị trí việc làm**

a) Địa điểm làm việc: Số 02 Trần Phú, Hà Đông, Hà Nội

b) Bộ phận/Đơn vị quản lý: Bộ môn Kiểm nghiệm thuốc và độc chất kiêm nhiệm công tác tại Bộ môn Bào chế-Công nghiệp dược, Bộ môn Thực vật-Dược liệu thuộc Khoa Dược, Viện Nghiên cứu Y-Dược cổ truyền Tuệ Tĩnh, Học viện Y - Dược học cổ truyền Việt Nam.

c) Vị trí việc làm: Giảng viên (hợp đồng lao động)

d) Nhiệm vụ: Thực hiện nhiệm vụ của giảng viên hạng III theo quy định hiện hành và theo sự phân công của lãnh đạo đơn vị. Thực hiện các nhiệm vụ khác theo sự phân công của Học viện Y - Dược học cổ truyền Việt Nam.

## **Điều 2. Quyền và nghĩa vụ của Bên B**

Ngoài thực hiện các quyền, nghĩa vụ theo quy định của pháp luật về lao động và quy định của pháp luật khác có liên quan, bên B còn thực hiện các quyền, nghĩa vụ sau:

### **1. Quyền của Bên B**

a) Tiền lương, thưởng và các khoản phụ cấp, bổ sung khác

- Mức lương tháng: Người lao động hưởng 100% mức lương tương đương chức danh nghề nghiệp Giảng viên (hạng III), bậc 3, hệ số 3,00.



- Thời gian tính nâng bậc lương lần sau kể từ ngày: 01 tháng 12 năm 2024
- Hình thức trả lương (tiền mặt/chuyển khoản): Qua thẻ ATM
- Kỳ hạn trả lương: một tháng một lần
- Tiền lương được trả vào: vào các ngày 10 - 15 hàng tháng
- Chế độ nâng bậc, nâng lương (ghi rõ thời gian, điều kiện và các trường hợp được nâng bậc, nâng lương nếu có): Theo quy định của Học viện.
- Thưởng (ghi rõ điều kiện và các trường hợp được thưởng, mức thưởng nếu có): Theo quy định của Học viện.
- Tiền tàu xe về nơi cư trú của bên B (ghi rõ các trường hợp được hỗ trợ tiền tàu xe về nơi cư trú, mức hỗ trợ) (nếu có): Người lao động tự túc.
- Hỗ trợ nâng cao trình độ chuyên môn, nghiệp vụ (nếu có): Theo quy định của Học viện.

b) Thời giờ làm việc, thời giờ nghỉ ngơi

- Thời giờ làm việc: 08 giờ/ngày, 05 ngày/tuần
- Thời giờ bên B được nghỉ liên tục trong ngày: Theo quy định hiện hành.
- Ngày nghỉ hằng tuần: Theo quy định hiện hành.
- Ngày nghỉ hằng năm: Theo quy định hiện hành.
- Ngày nghỉ lễ, Tết: Theo quy định hiện hành.

c) Điều kiện lao động

- Bên B được cung cấp (miễn phí) trang thiết bị bảo hộ lao động phù hợp với công việc và được bên A bảo đảm an toàn lao động, vệ sinh lao động trong thời gian làm việc theo hợp đồng. Bên B có trách nhiệm sử dụng, bảo quản các trang thiết bị bảo hộ lao động và tuân thủ các quy định về an toàn lao động, vệ sinh lao động.
- Bên B có trách nhiệm tham gia và được hưởng các chế độ bảo hiểm xã hội, bảo hiểm y tế, bảo hiểm thất nghiệp và các loại bảo hiểm khác theo quy định của pháp luật.

Mức đóng của các bên cụ thể như sau: Theo quy định hiện hành.

## 2. Nghĩa vụ của bên B

- a) Thực hiện các nhiệm vụ theo thỏa thuận trong hợp đồng lao động.
- b) Cung cấp văn bản, giấy tờ xác minh đủ tiêu chuẩn, điều kiện thực hiện công việc thỏa thuận theo yêu cầu của bên A.
- c) Chấp hành quy định, nội quy, quy chế của Học viện Y-Dược học cổ truyền Việt Nam, kỷ luật làm việc và các quy định pháp luật.
- d) Chấp hành việc xử lý vi phạm kỷ luật lao động và trách nhiệm bồi thường, hoàn trả theo quy định của pháp luật.
- đ) Tuân thủ các quy định về bảo mật theo yêu cầu của bên A.
- e) Chấp hành sự quản lý, điều hành, giám sát của người sử dụng lao động.



g) Thuê thu nhập cá nhân (nếu có) do bên B đóng. Học viện Y-Dược học cổ truyền Việt Nam sẽ tạm khấu trừ trước khi chi trả cho bên B theo quy định.

### **Điều 3. Quyền và nghĩa vụ của bên A**

#### **1. Quyền của bên A**

- a) Yêu cầu bên B thực hiện công việc và tuân thủ các nghĩa vụ theo đúng thỏa thuận tại hợp đồng này.
- b) Trường hợp bên B vi phạm nghĩa vụ thì bên A có quyền đơn phương chấm dứt thực hiện hợp đồng và yêu cầu bồi thường thiệt hại.

#### **2. Nghĩa vụ của bên A**

- a) Chi trả lương, thực hiện chế độ, chính sách khác cho người lao động theo thỏa thuận bảo đảm phù hợp với quy định của pháp luật lao động và quy định của pháp luật khác có liên quan.
- b) Cung cấp thông tin, tài liệu và các phương tiện, điều kiện làm việc cần thiết để bên B thực hiện công việc.
- c) Bảo đảm quyền, lợi ích hợp pháp của người lao động theo thỏa thuận tại hợp đồng và quy định của pháp luật về lao động.

### **Điều 4. Tạm hoãn, chấm dứt hợp đồng lao động**

1. Việc tạm hoãn, chấm dứt hợp đồng giữa các bên được thực hiện theo quy định của pháp luật về lao động.

2. Bên B bị coi là vi phạm hợp đồng khi thuộc một trong các trường hợp sau đây:

- a) Bên B không thực hiện hoặc thực hiện không đúng, không đầy đủ và chậm thực hiện bất kỳ nghĩa vụ nào quy định trong hợp đồng này.
- b) Bên B vi phạm kỷ luật lao động.
- c) Đơn phương chấm dứt hợp đồng trái quy định.

3. Trường hợp bên A vi phạm nghiêm trọng nghĩa vụ thì bên B có quyền đơn phương chấm dứt thực hiện hợp đồng và yêu cầu bồi thường thiệt hại.

4. Trong thời gian thử việc, nếu bên B không đáp ứng được yêu cầu thì bên A có quyền chấm dứt hợp đồng lao động với bên B trước thời hạn.

### **Điều 5. Phương thức giải quyết tranh chấp**

Trong quá trình thực hiện hợp đồng, nếu có vấn đề phát sinh cần giải quyết thì hai bên thỏa thuận và thống nhất giải quyết kịp thời, bảo đảm phù hợp với các quy định của pháp luật. Trường hợp không thỏa thuận được thì một trong các bên có quyền khởi kiện yêu cầu giải quyết tại Tòa án có thẩm quyền theo quy định của pháp luật.

### **Điều 6. Điều khoản thi hành**

a) Hợp đồng có hiệu lực từ ngày 01 tháng 12 năm 2024

b) Trong quá trình thực hiện hợp đồng lao động, nếu bên nào có yêu cầu sửa đổi, bổ sung nội dung hợp đồng thì phải báo cho bên kia biết trước ít nhất 03 ngày làm việc về nội dung cần sửa đổi, bổ sung.



Trường hợp hai bên thỏa thuận được thì việc sửa đổi, bổ sung nội dung hợp đồng lao động được tiến hành bằng việc ký kết phụ lục hợp đồng lao động hoặc ký kết hợp đồng lao động mới.

Trường hợp hai bên không thỏa thuận được việc sửa đổi, bổ sung nội dung hợp đồng lao động thì tiếp tục thực hiện hợp đồng lao động đã ký kết.

c) Những vấn đề về lao động khác không ghi trong hợp đồng này được thực hiện theo quy định tại Bộ luật Lao động và các văn bản quy phạm pháp khác có liên quan.

d) Hợp đồng được làm thành 03 bản có giá trị pháp lý như nhau, mỗi bên giữ 01 bản, 01 bản lưu trong hồ sơ của bên B. / *mb*

**Bên A**

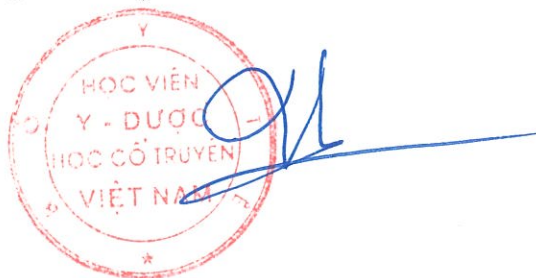
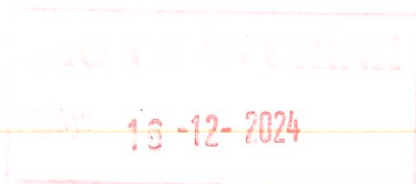


**Nguyễn Quốc Huy**

**Bên B**

*Handwritten signature*

**Trần Thị Phương**



**PHỤ TRÁCH PHÒNG HÀNH CHÍNH TỔNG HỢP  
Nguyễn Vinh Huy Chính**



1000 1000 1000  
1000 1000 1000

BỘ Y TẾ  
HỌC VIỆN YDHCT VIỆT NAM

CỘNG HÒA XÃ HỘI CHỦ NGHĨA VIỆT NAM  
Độc lập - Tự do - Hạnh phúc

Số: 20 /HDLĐ

Hà Nội, ngày 13 tháng 12 năm 2023

**HỢP ĐỒNG LAO ĐỘNG  
THỰC HIỆN CÔNG VIỆC CHUYÊN MÔN, NGHIỆP VỤ**

*Căn cứ Bộ luật Lao động ngày 20 tháng 11 năm 2019;*

*Căn cứ Nghị định số 111/2022/NĐ-CP ngày 30 tháng 12 năm 2022 của Chính phủ về hợp đồng đối với một số loại công việc trong cơ quan hành chính và đơn vị sự nghiệp công lập;*

*Căn cứ nhu cầu và khả năng thực tế của các bên trong hợp đồng;*

Hôm nay, ngày 13 tháng 12 năm 2023 tại Học viện Y-Dược học cổ truyền Việt Nam, chúng tôi gồm các bên dưới đây:

**BÊN A: NGƯỜI SỬ DỤNG LAO ĐỘNG**

Cơ quan, đơn vị: Học viện Y-Dược học cổ truyền Việt Nam

(sau đây viết tắt là Học viện).

Địa chỉ: Số 2 Trần Phú, Hà Đông, Hà Nội

Điện thoại: 024.33824930

Tài khoản ngân hàng: Ngân hàng Thương mại cổ phần Công thương Việt Nam

Đại diện theo pháp luật: Ông Nguyễn Quốc Huy

Chức vụ: Giám đốc Học viện

**BÊN B: NGƯỜI LAO ĐỘNG**

Bà Trần Thị Phương

Sinh ngày 24 tháng 02 năm 1988 tại Bắc Giang

Giới tính: Nữ

Địa chỉ nơi cư trú: TDP Đồng Quán, Thị trấn Bồ Hạ, Yên Thế, tỉnh Bắc Giang

Điện thoại: 0866653197

Mã số thuế (nếu có):

Tài khoản ngân hàng: 100880553391

Nơi mở tài khoản: Ngân hàng Vietinbank

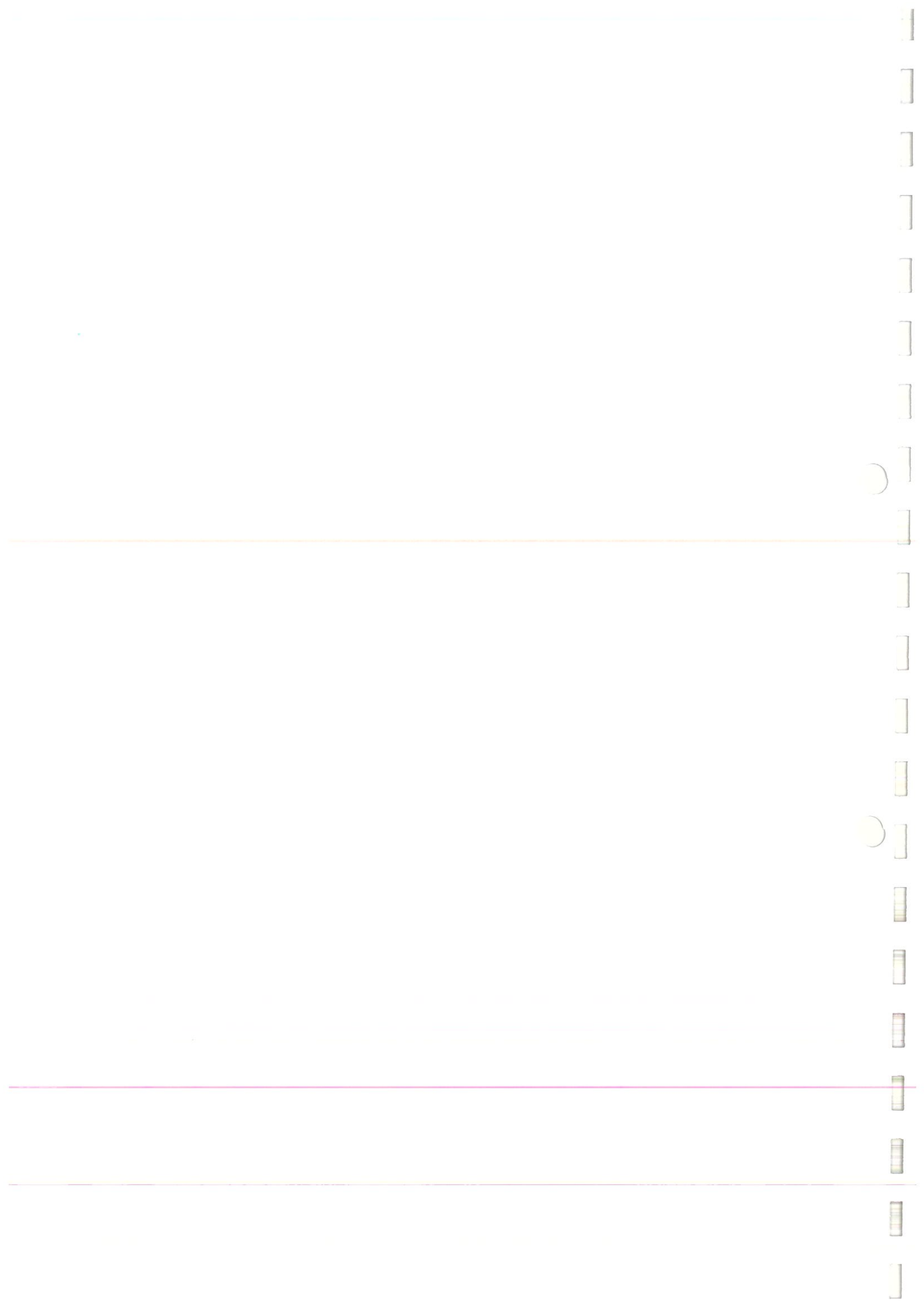
Email (nếu có): phuongtran24288@gmail.com

Số CMND/CCCD/Hộ chiếu: 024188017586

Cấp ngày: 10 tháng 11 năm 2023

Tại: Cục Cảnh sát QLHC về TTXH

Trình độ chuyên môn: Tiến sĩ chuyên ngành dược





Chuyên ngành đào tạo: Dược

Trình độ tin học:

Trình độ ngoại ngữ: Tiếng Hàn TOPIK 4

Hai bên thỏa thuận ký kết hợp đồng lao động và cam kết thực hiện những nội dung sau đây:

## **Điều 1. Công việc, vị trí việc làm và thời hạn hợp đồng**

### **1. Thời hạn hợp đồng**

Bên A và bên B thỏa thuận ký kết hợp đồng xác định thời hạn, cụ thể như sau:

Thời hạn của hợp đồng lao động: 12 tháng, kể từ ngày 13 tháng 12 năm 2023 đến ngày 12 tháng 12 năm 2024.

Trong thời hạn 30 ngày kể từ ngày hợp đồng lao động này hết hạn, bên A và bên B phải thỏa thuận để ký kết hợp đồng lao động mới; trong thời gian chưa ký kết hợp đồng lao động mới thì quyền, nghĩa vụ và lợi ích của hai bên được thực hiện theo hợp đồng này.

Trường hợp bên A và bên B tiếp tục thỏa thuận ký kết hợp đồng lao động mới là hợp đồng xác định thời hạn thì chỉ được ký thêm 01 lần. Hết thời hạn ký kết hợp đồng lần thứ 2, nếu bên B vẫn tiếp tục làm việc thì phải ký kết hợp đồng lao động không xác định thời hạn.

Trường hợp hết thời hạn 30 ngày kể từ ngày hợp đồng lao động này hết hạn mà bên A và bên B không ký kết hợp đồng lao động mới và không có thỏa thuận khác thì hợp đồng này đương nhiên trở thành hợp đồng lao động không xác định thời hạn.

### **2. Công việc và vị trí việc làm**

a) Địa điểm làm việc: Số 02 Trần Phú, Hà Đông, Hà Nội

b) Bộ phận/Đơn vị quản lý: Bộ môn Kiểm nghiệm thuốc và độc chất kiêm nhiệm công tác tại Bộ môn Bào chế-Công nghiệp dược, Bộ môn Thực vật-Dược liệu thuộc Khoa Dược, Viện Nghiên cứu Y-Dược cổ truyền Tuệ Tĩnh, Học viện Y - Dược học cổ truyền Việt Nam.

c) Vị trí việc làm: Giảng viên hợp đồng

d) Nhiệm vụ: Thực hiện nhiệm vụ của giảng viên theo quy định hiện hành và theo sự phân công của lãnh đạo đơn vị. Thực hiện các nhiệm vụ khác theo sự phân công của Học viện Y - Dược học cổ truyền Việt Nam.

## **Điều 2. Quyền và nghĩa vụ của Bên B**

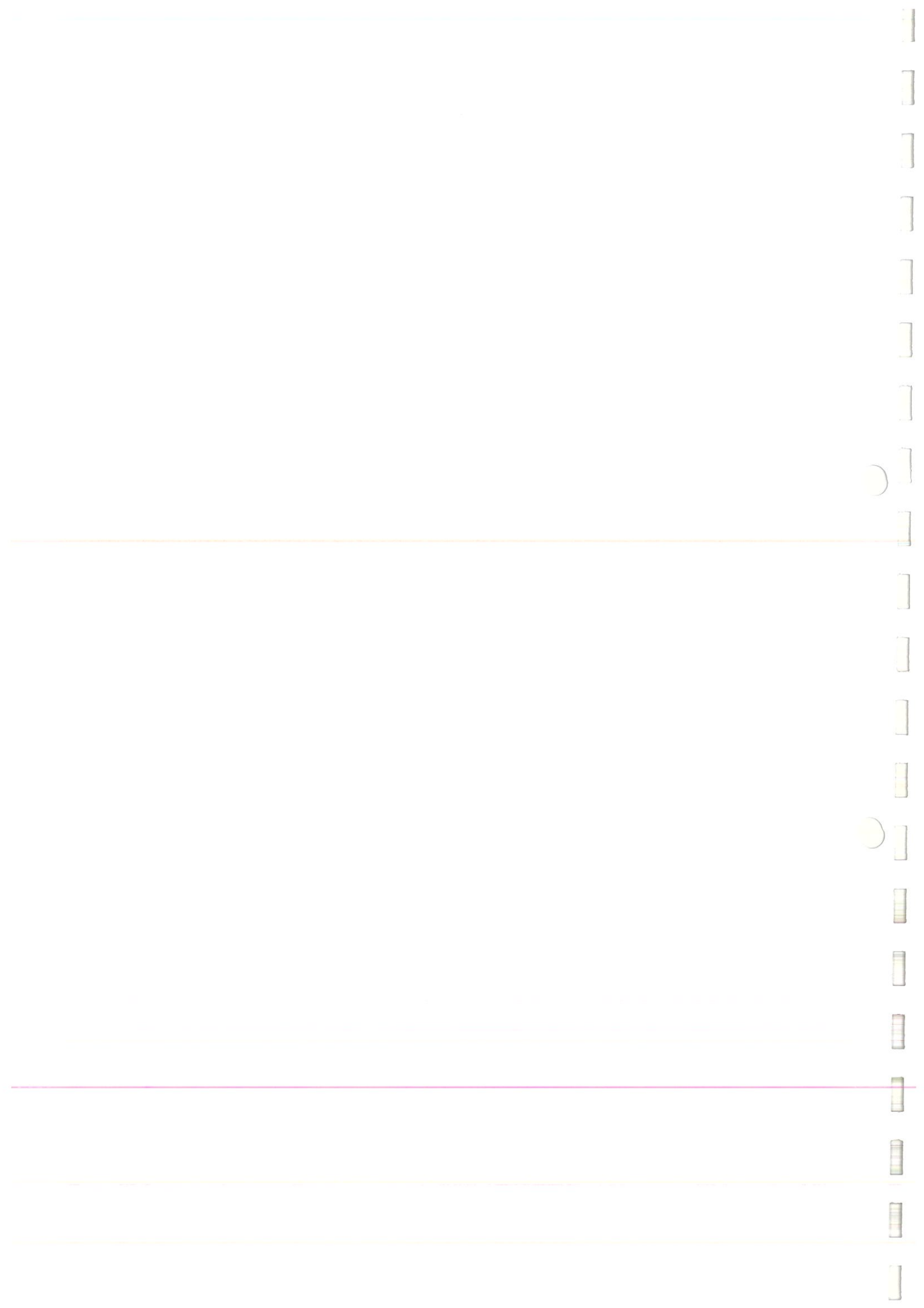
Ngoài thực hiện các quyền, nghĩa vụ theo quy định của pháp luật về lao động và quy định của pháp luật khác có liên quan, bên B còn thực hiện các quyền, nghĩa vụ sau:

### **1. Quyền của Bên B**

a) Tiền lương, thưởng và các khoản phụ cấp, bổ sung khác

- Mức lương tháng: Người lao động hưởng 85% mức lương tương đương bậc 3, chức danh nghề nghiệp Giảng viên (hạng III), hệ số 3,00.

- Hình thức trả lương (tiền mặt/chuyển khoản): Qua thẻ ATM



- Kỳ hạn trả lương: một tháng một lần
- Tiền lương được trả vào: vào các ngày 10 - 15 hàng tháng
- Chế độ nâng bậc, nâng lương (ghi rõ thời gian, điều kiện và các trường hợp được nâng bậc, nâng lương nếu có): Theo quy định của Học viện.
- Thưởng (ghi rõ điều kiện và các trường hợp được thưởng, mức thưởng nếu có): Theo quy định của Học viện.
- Tiền tàu xe về nơi cư trú của bên B (ghi rõ các trường hợp được hỗ trợ tiền tàu xe về nơi cư trú, mức hỗ trợ) (nếu có): Người lao động tự túc.
- Hỗ trợ nâng cao trình độ chuyên môn, nghiệp vụ (nếu có): Theo quy định của Học viện.

b) Thời giờ làm việc, thời giờ nghỉ ngơi

- Thời giờ làm việc: 08 giờ/ngày, 05 ngày/tuần
- Thời giờ bên B được nghỉ liên tục trong ngày: Theo quy định hiện hành.
- Ngày nghỉ hằng tuần: Theo quy định hiện hành.
- Ngày nghỉ hằng năm: Theo quy định hiện hành.
- Ngày nghỉ lễ, Tết: Theo quy định hiện hành.

c) Điều kiện lao động

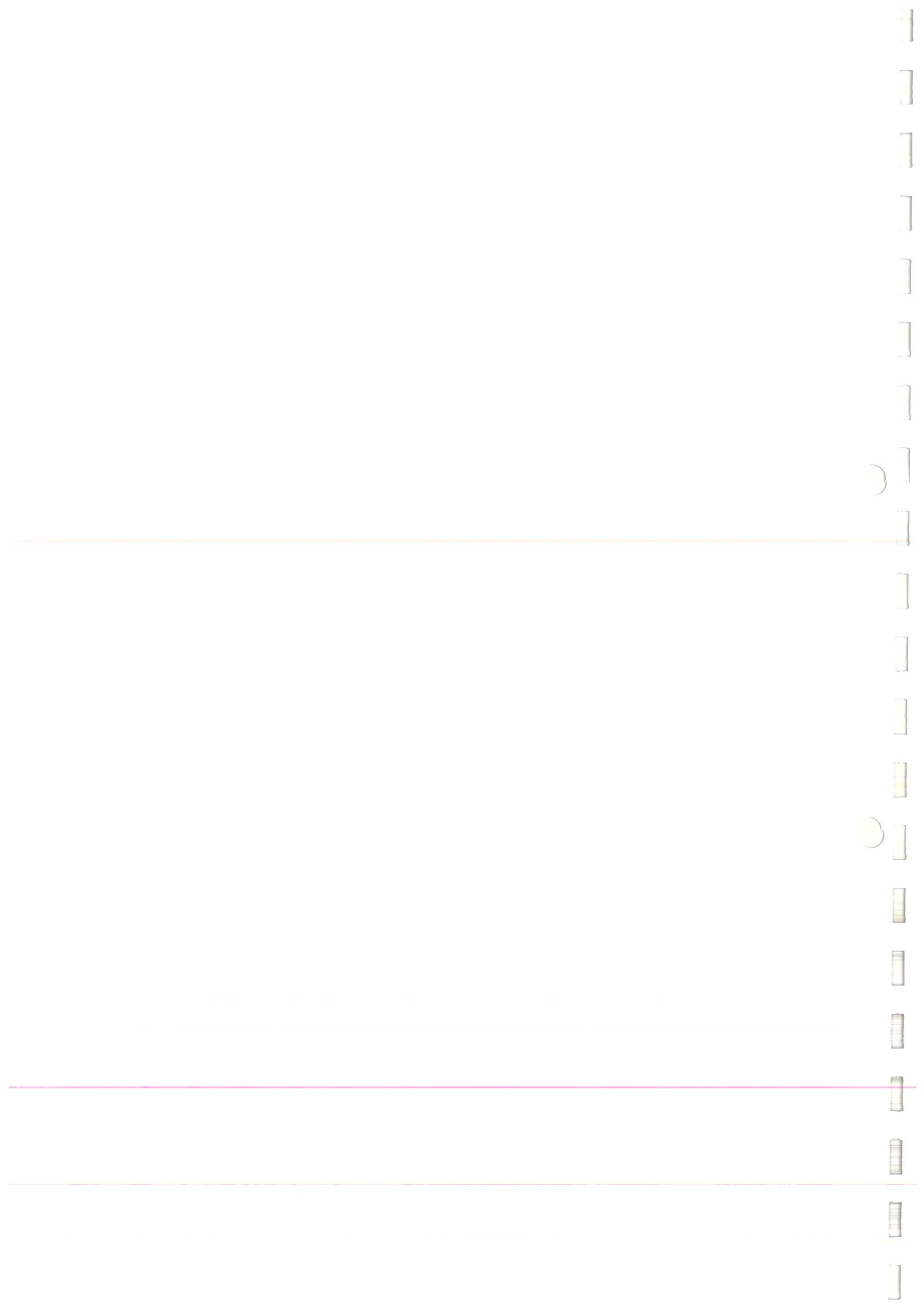
- Bên B được cung cấp (miễn phí) trang thiết bị bảo hộ lao động phù hợp với công việc và được bên A bảo đảm an toàn lao động, vệ sinh lao động trong thời gian làm việc theo hợp đồng. Bên B có trách nhiệm sử dụng, bảo quản các trang thiết bị bảo hộ lao động và tuân thủ các quy định về an toàn lao động, vệ sinh lao động.
- Bên B có trách nhiệm tham gia và được hưởng các chế độ bảo hiểm xã hội, bảo hiểm y tế, bảo hiểm thất nghiệp và các loại bảo hiểm khác theo quy định của pháp luật.

Mức đóng của các bên cụ thể như sau: Theo quy định hiện hành.

**2. Nghĩa vụ của bên B**

- a) Thực hiện các nhiệm vụ theo thỏa thuận trong hợp đồng lao động.
- b) Cung cấp văn bản, giấy tờ xác minh đủ tiêu chuẩn, điều kiện thực hiện công việc thỏa thuận theo yêu cầu của bên A.
- c) Chấp hành quy định, nội quy, quy chế của Học viện Y-Dược học cổ truyền Việt Nam, kỷ luật làm việc và các quy định pháp luật.
- d) Chấp hành việc xử lý vi phạm kỷ luật lao động và trách nhiệm bồi thường, hoàn trả theo quy định của pháp luật.
- đ) Tuân thủ các quy định về bảo mật theo yêu cầu của bên A.
- e) Chấp hành sự quản lý, điều hành, giám sát của người sử dụng lao động.
- g) Thuê thu nhập cá nhân (nếu có) do bên B đóng. Học viện Y-Dược học cổ truyền Việt Nam sẽ tạm khấu trừ trước khi chi trả cho bên B theo quy định.

**Điều 3. Quyền và nghĩa vụ của bên A**





### 1. Quyền của bên A

- a) Yêu cầu bên B thực hiện công việc và tuân thủ các nghĩa vụ theo đúng thỏa thuận tại hợp đồng này.
- b) Trường hợp bên B vi phạm nghĩa vụ thì bên A có quyền đơn phương chấm dứt thực hiện hợp đồng và yêu cầu bồi thường thiệt hại.

### 2. Nghĩa vụ của bên A

- a) Chi trả lương, thực hiện chế độ, chính sách khác cho người lao động theo thỏa thuận bảo đảm phù hợp với quy định của pháp luật lao động và quy định của pháp luật khác có liên quan.
- b) Cung cấp thông tin, tài liệu và các phương tiện, điều kiện làm việc cần thiết để bên B thực hiện công việc.
- c) Bảo đảm quyền, lợi ích hợp pháp của người lao động theo thỏa thuận tại hợp đồng và quy định của pháp luật về lao động.

### Điều 4. Tạm hoãn, chấm dứt hợp đồng lao động

1. Việc tạm hoãn, chấm dứt hợp đồng giữa các bên được thực hiện theo quy định của pháp luật về lao động.

2. Bên B bị coi là vi phạm hợp đồng khi thuộc một trong các trường hợp sau đây:

- a) Bên B không thực hiện hoặc thực hiện không đúng, không đầy đủ và chậm thực hiện bất kỳ nghĩa vụ nào quy định trong hợp đồng này.
- b) Bên B vi phạm kỷ luật lao động.
- c) Đơn phương chấm dứt hợp đồng trái quy định.

3. Trường hợp bên A vi phạm nghiêm trọng nghĩa vụ thì bên B có quyền đơn phương chấm dứt thực hiện hợp đồng và yêu cầu bồi thường thiệt hại.

4. Trong thời gian thử việc, nếu bên B không đáp ứng được yêu cầu thì bên A có quyền chấm dứt hợp đồng lao động với bên B trước thời hạn.

### Điều 5. Phương thức giải quyết tranh chấp

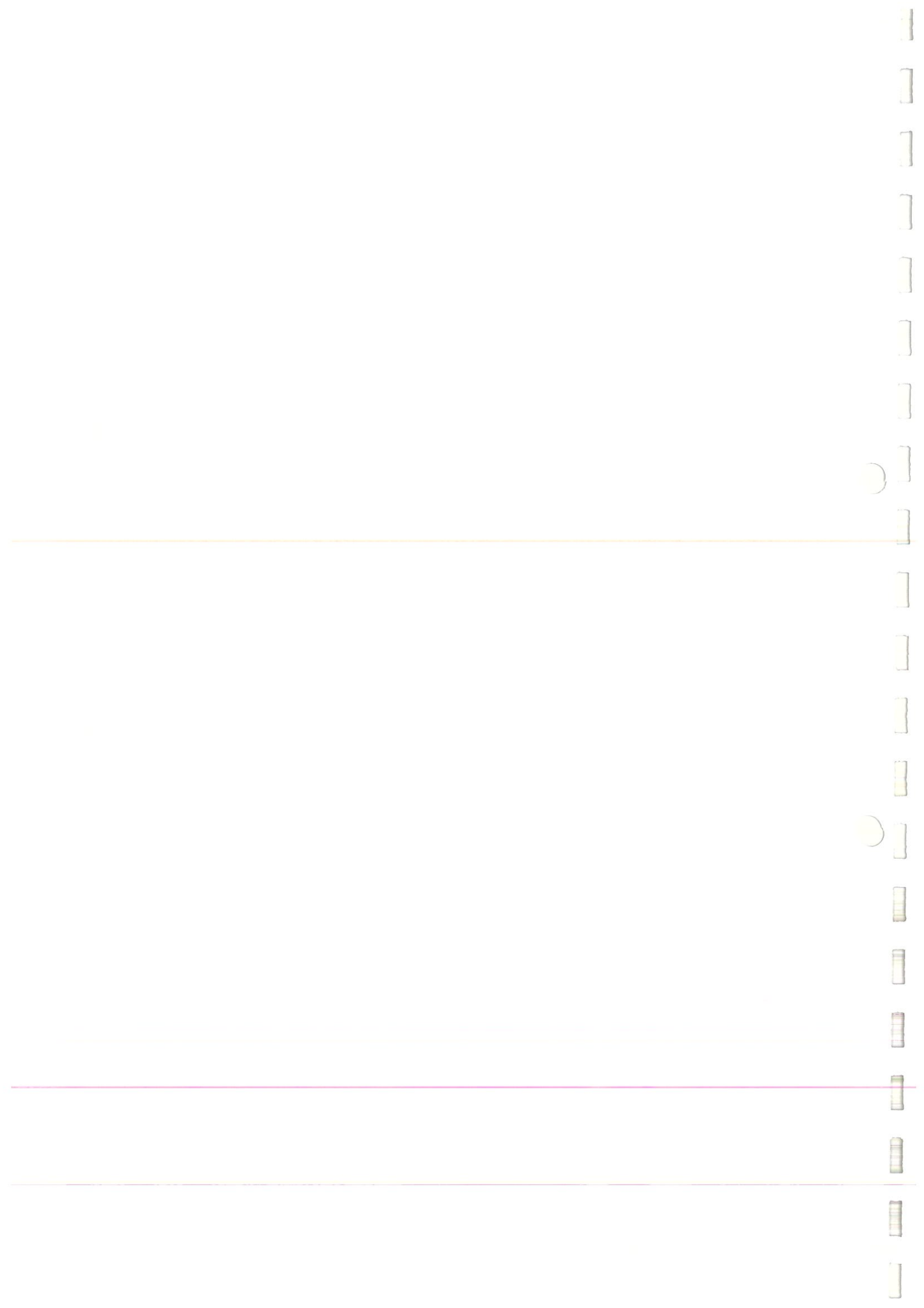
Trong quá trình thực hiện hợp đồng, nếu có vấn đề phát sinh cần giải quyết thì hai bên thỏa thuận và thống nhất giải quyết kịp thời, bảo đảm phù hợp với các quy định của pháp luật. Trường hợp không thỏa thuận được thì một trong các bên có quyền khởi kiện yêu cầu giải quyết tại Tòa án có thẩm quyền theo quy định của pháp luật.

### Điều 6. Điều khoản thi hành

a) Hợp đồng có hiệu lực từ ngày 13 tháng 12 năm 2023

b) Trong quá trình thực hiện hợp đồng lao động, nếu bên nào có yêu cầu sửa đổi, bổ sung nội dung hợp đồng thì phải báo cho bên kia biết trước ít nhất 03 ngày làm việc về nội dung cần sửa đổi, bổ sung.

Trường hợp hai bên thỏa thuận được thì việc sửa đổi, bổ sung nội dung hợp đồng lao động được tiến hành bằng việc ký kết phụ lục hợp đồng lao động hoặc ký kết hợp đồng lao động mới.





Trường hợp hai bên không thỏa thuận được việc sửa đổi, bổ sung nội dung hợp đồng lao động thì tiếp tục thực hiện hợp đồng lao động đã ký kết.

c) Những vấn đề về lao động khác không ghi trong hợp đồng này được thực hiện theo quy định tại Bộ luật Lao động và các văn bản quy phạm pháp khác có liên quan.

d) Hợp đồng được làm thành 03 bản có giá trị pháp lý như nhau, mỗi bên giữ 01 bản, 01 bản lưu trong hồ sơ của bên B. / *phần*

Bên A



Nguyễn Quốc Huy

Bên B

*Trần Thị Phương*





APRIL 2024

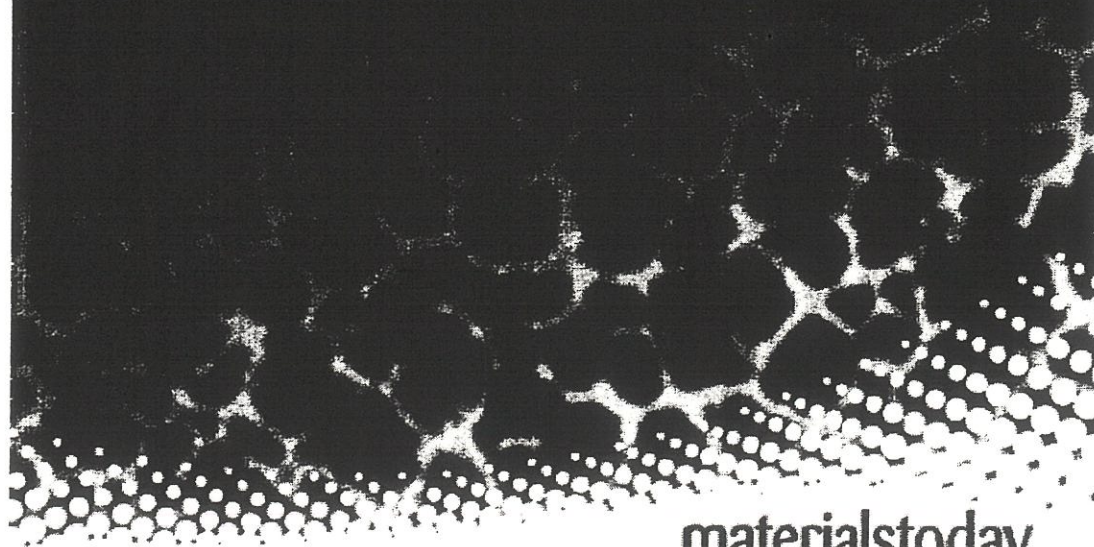
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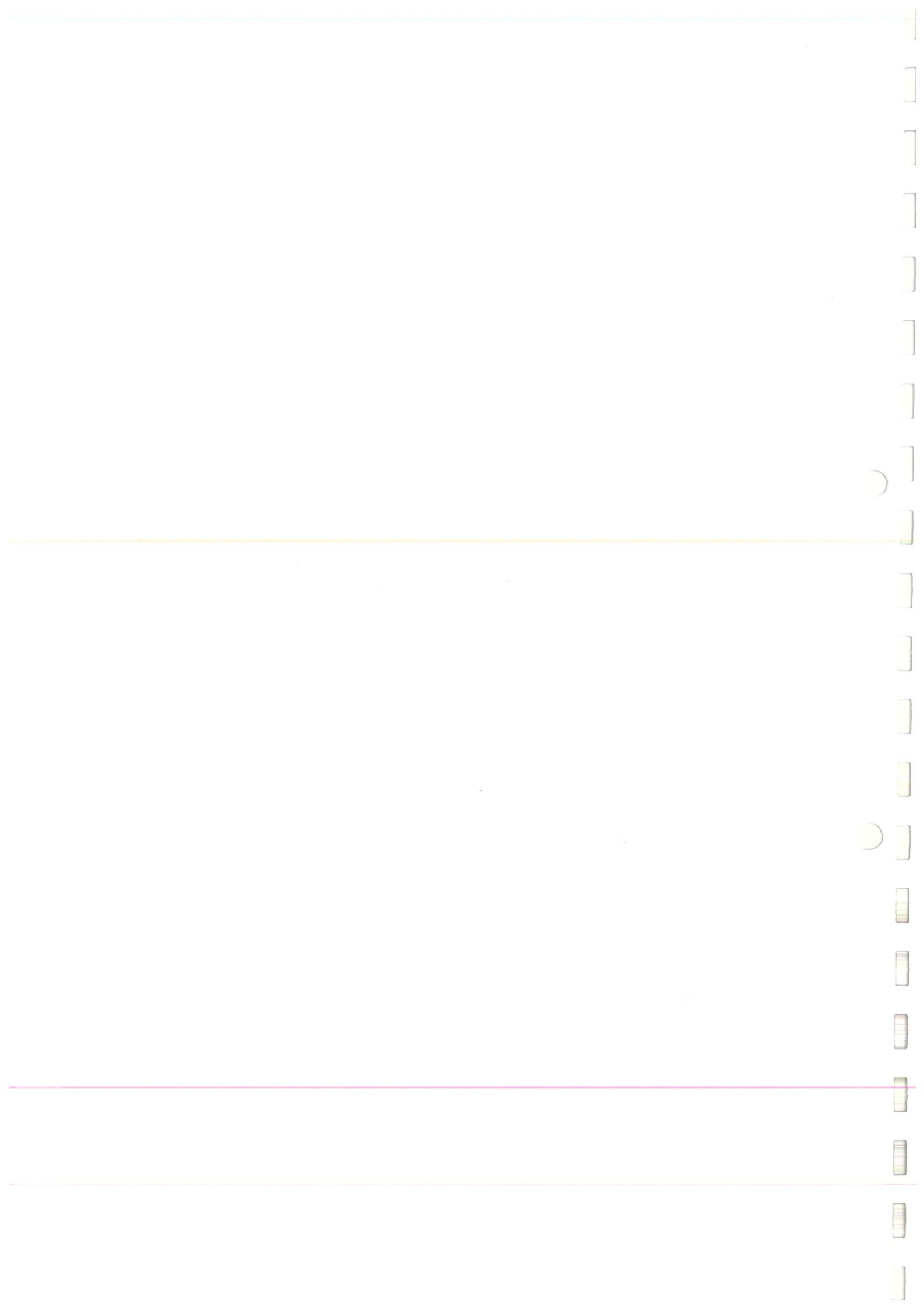
# BIOMATERIALS ADVANCES

Guest Editor

Professor Manuel Salmeron-Sanchez



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## Sialic acid-decorated liposomes enhance the anti-cancer efficacy of docetaxel in tumor-associated macrophages

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### ARTICLE INFO

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Sialic acid  
Tumor microenvironment  
Tumor-associated macrophages

### ABSTRACT

Tumor-associated macrophages (TAMs) in the tumor microenvironment potentially enhance tumor growth and invasion through various mechanisms and are thus an essential factor in tumor immunity. The highly expressed siglec-1 receptors on the surfaces of TAMs are potential targets for cancer drug delivery systems. Sialic acid (SA) is a specific ligand for siglec-1. In this study, the sialic acid-polyethylene glycol conjugate (DSPE-PEG<sub>2000</sub>-SA) was synthesized to modify the surface of liposomes and target TAMs by interacting with the siglec-1 receptor. Three docetaxel (DTX)-loaded liposomes, conventional (DTX-CL), DSPE-PEG<sub>2000</sub>-coated (DTX-PL), and DSPE-PEG<sub>2000</sub>-SA-coated (DTX-SAPL) liposomes, were prepared, with a particle size of <100 nm, uniform polydispersity index (PDI) values, negative zeta potential, and % encapsulation efficiency (EE) exceeding 95 %. Liposomes showed high stability after 3 months of storage at 4 °C without significant changes in particle size, PDI, zeta potential, or % EE. DTX was released from liposomes according to the Weibull model, and DTX-SAPL exhibited more rapid drug release than other liposomes. *In vitro* studies demonstrated that DTX-SAPL liposome exhibited a higher uptake and cytotoxicity on RAW 264.7 cells (TAM model) and lower toxicity on NIH3T3 cells (normal cell model) than other formulations. The high cell uptake ability was demonstrated by the role of the SA-SA receptor. Biodistribution studies indicated a high tumor accumulation of surface-modified liposomal formulations, particularly SA-modified liposomes, showing high signal accumulation at the tumor periphery, where TAMs were highly concentrated. *Ex vivo* imaging showed a significantly higher accumulation of SA-modified liposomes in the tumor, kidney, and heart than conventional liposomes. In the anti-cancer efficacy study, DTX-SAPL liposomes showed effective inhibition of tumor growth and relatively low systemic toxicity, as evidenced by the tumor volume, tumor weight, body weight values, and histopathological analysis. Therefore, DSPE-PEG<sub>2000</sub>-SA-coated liposomes could be promising carriers for DTX delivery targeting TAMs in cancer therapy.

### 1. Introduction

Targeted drug delivery systems have recently garnered a lot of attention in cancer therapy. The underlying mechanism of these systems is selective drug delivery to the tumor site, which improves drug effectiveness and reduces toxicity [1]. In addition, enhanced permeation and retention (EPR) aids drug delivery to tumors [1,2]. However, the efficacy of cancer therapy based on EPR is controversial because its permeability is limited at the tumor site. The extracellular matrix stiffness and selective pressures from the tumor microenvironment (TME) complicate the delivery of nanoparticles to the blood vessels and cancer

cells [3].

The TME comprises numerous immune cell types, such as mast cells, neutrophils, and tumor-associated macrophages (TAMs), which account for approximately 50 % of the total tumor volume [4,5]. Unlike normal macrophages, TAMs are nontumor-immunoreactive and incapable of inhibiting tumor growth. Instead, they secrete factors that promote tumor immunosuppression and facilitate tumor proliferation and invasion [6]. Owing to the aforementioned characteristics, targeting TAMs could be an effective immunotherapy approach in the treatment of tumors.

A common approach toward enhancing the permeation and targeting

\* Corresponding author.

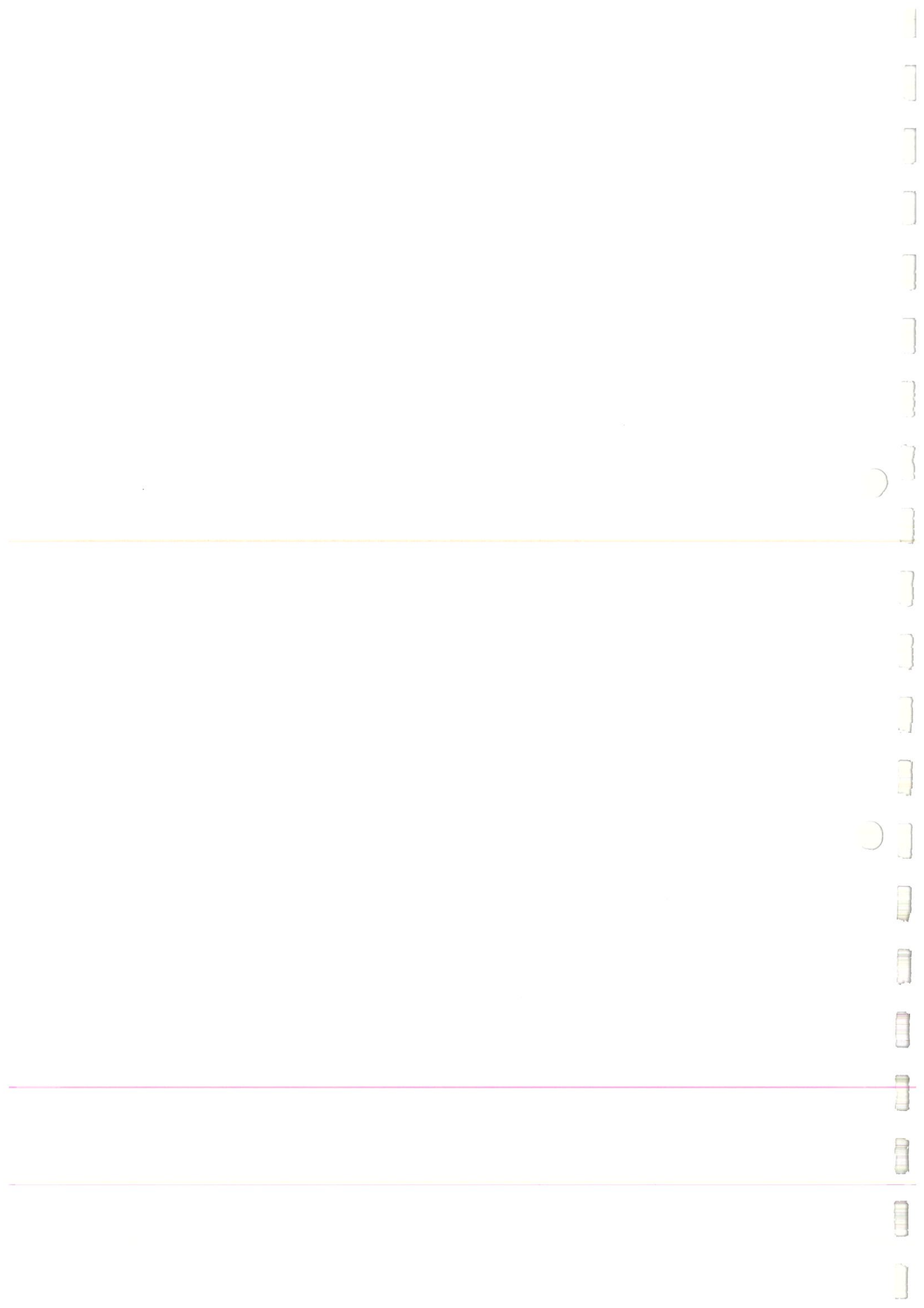
E-mail address: [eicosa@cnu.ac.kr](mailto:eicosa@cnu.ac.kr) (J.-S. Park).

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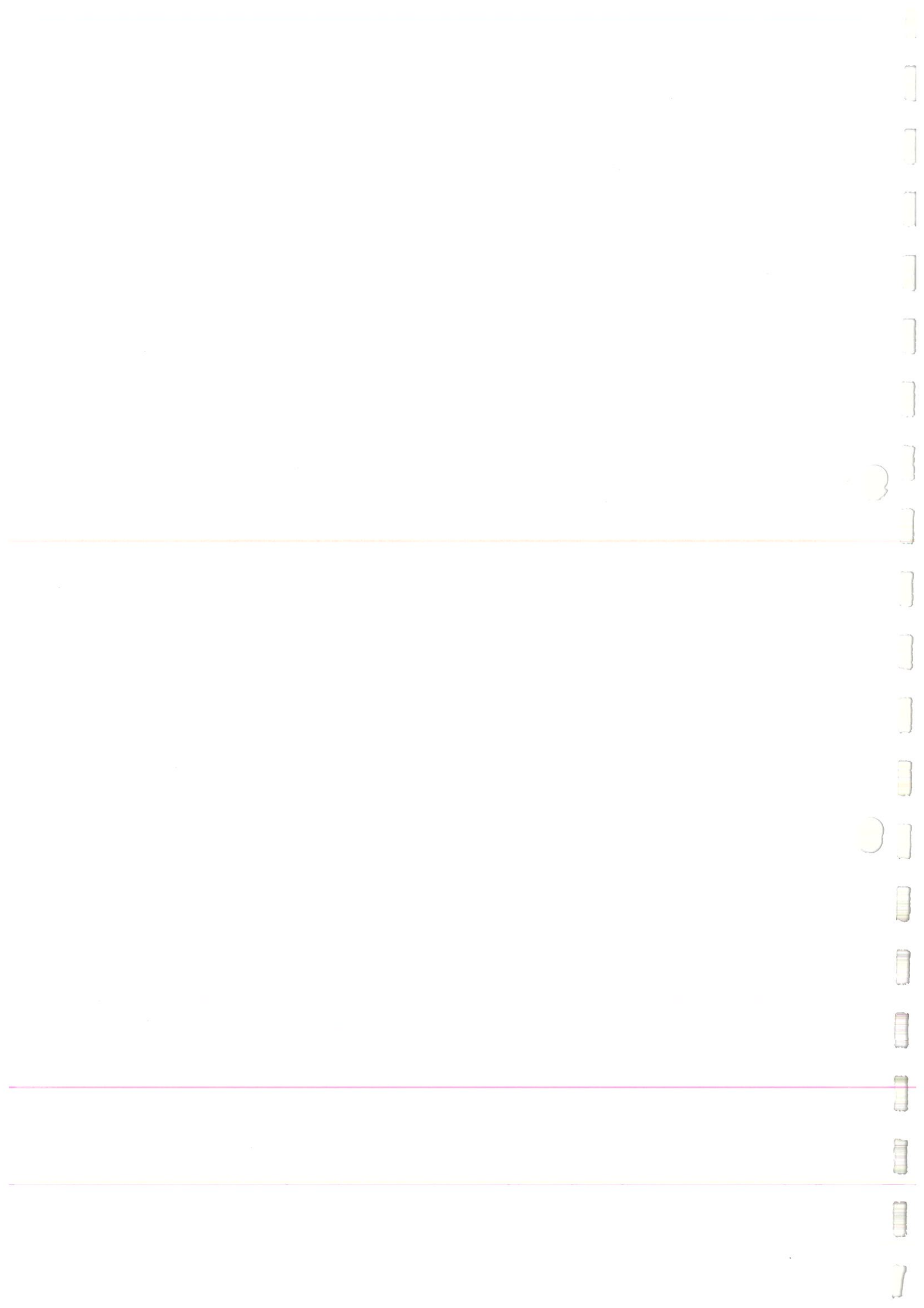
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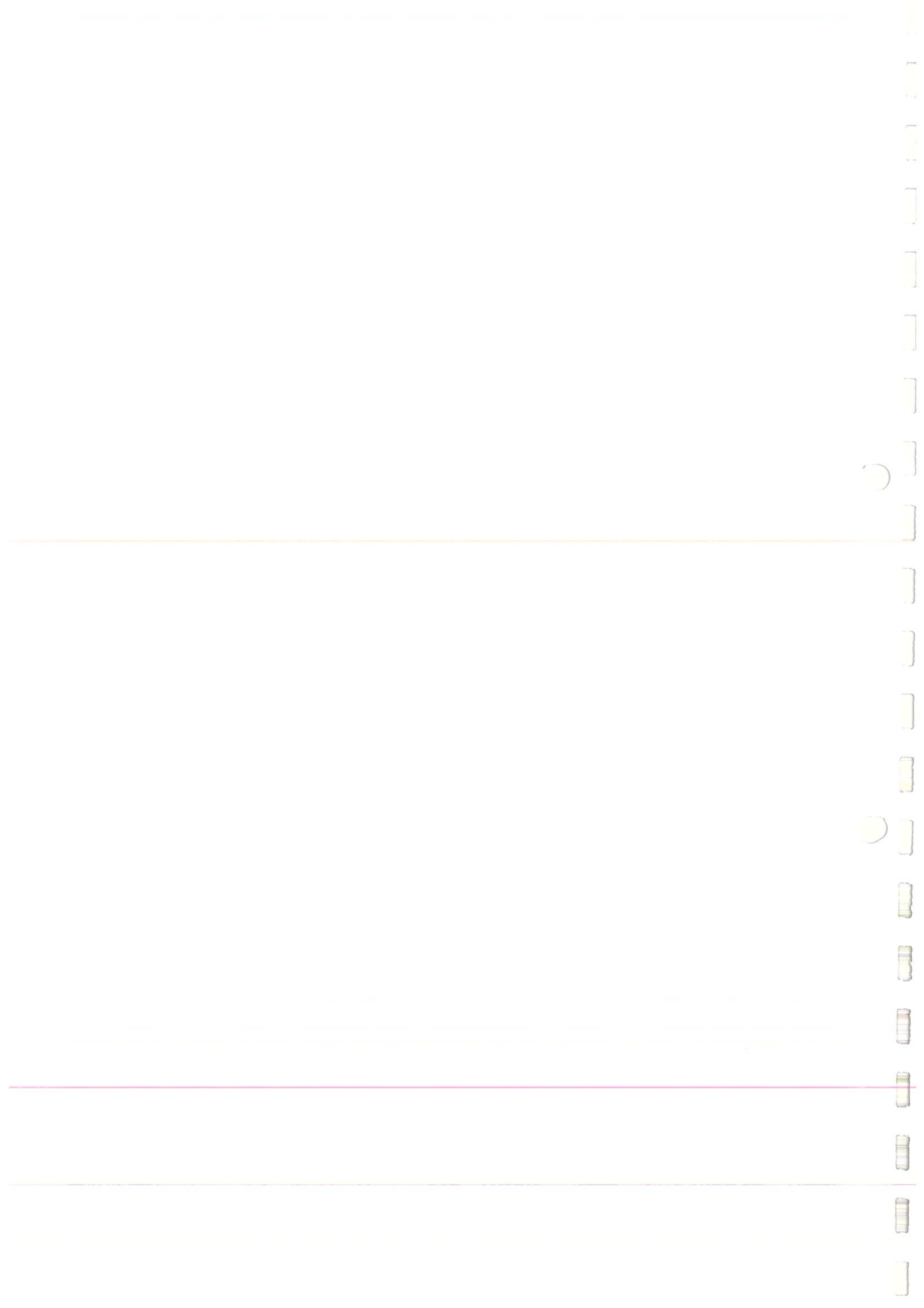
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# Solid dispersion of mebendazole via surfactant carrier to improve oral bioavailability and in vitro anticancer efficacy

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## Abstract

**Purpose** This study aimed to prepare a solid dispersion (SD) formulation of MBZ to improve dissolution and oral bioavailability.

**Methods** A SD formulation of mebendazole (MBZ) was prepared using sodium dodecyl sulfate (SDS) as a carrier via lyophilization method. Powder X-ray diffraction (PXRD), differential scanning calorimetry (DSC), Fourier-transform infrared spectroscopy (FTIR), and scanning electron microscopy (SEM) were used to confirm the structural properties and morphology of the MBZ-SD formulation. Dissolution study was conducted in an acidic medium (0.1 M HCl), and pharmacokinetic study was conducted in rats. In addition, the in vitro anticancer effects of MBZ-SD were also investigated in various cancer cell lines.

**Results** From the results of PXRD, DSC, FTIR, and SEM assessments, there was an interaction between MBZ and SDS in the MBZ-SD. MBZ-SD significantly improved the aqueous solubility of MBZ (approximately 15,982-fold) and the dissolution of MBZ at 5 min (1.5-fold) as compared to that of pure MBZ. The area under the curve ( $AUC_{0-24}$ ) and the maximum concentration ( $C_{max}$ ) of the MBZ-SD formulation showed a 3.56- and 3.30-fold increased values compared to pure MBZ. The anticancer effects of MBZ with  $IC_{50}$  value were in the order of A549 > MDA-MB-231 > HepG2 > MCF-7 > NCI-H1299 > HeLa. At safe concentrations in normal cells, the MBZ-SD formulation exhibited the superior anticancer efficacy in HeLa cells.

**Conclusion** The obtained results in the present study suggests that SD is a good candidate for improving the bioavailability and anticancer effects of MBZ.

**Keywords** Mebendazole · Solid dispersion · Dissolution · Oral bioavailability · Anticancer effect

## Introduction

Mebendazole (MBZ) is a broad-spectrum anthelmintic drug, of the benzimidazole class that is used to treat ascariasis (roundworm infection), enterobiasis (pinworm infection), and hookworm infection caused by *Ancylostoma duodenale*, *Necator americanus*, and trichuriasis (whipworm infection) (Jongsuksuntigul et al. 1993; Flohr et al. 2007; Soukhatammavong et al. 2012). Recently, MBZ was reported to have anticancer properties that can inhibit the growth of

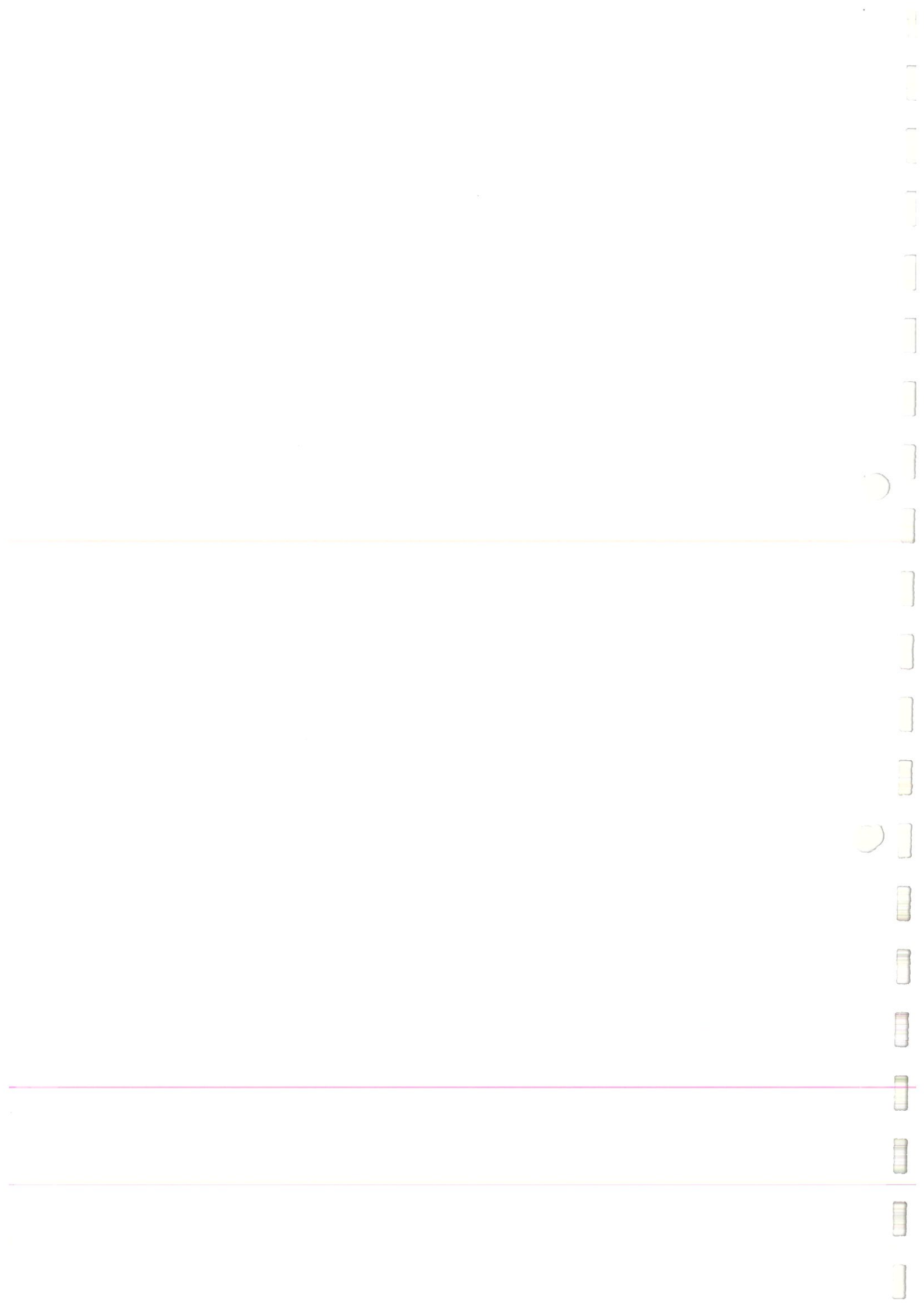
different types of cancer cells such as colon, stomach, adrenal, breast, and lung cancers (Mukhopadhyay et al. 2002; Sasaki et al. 2002; Martarelli et al. 2008; Doudican et al. 2008; Nygren et al. 2013; Pinto et al. 2015; Williamson et al. 2016; Shashaani et al. 2016; Zhang et al. 2019). It was reported that MBZ exhibits dose- and time-dependent apoptotic effects in human lung cancer cells (Mukhopadhyay et al. 2002). In another study by Pinto et al., high cytotoxicity of MBZ in gastric cancer cells was demonstrated with an  $IC_{50}$  of 0.39  $\mu$ M for ACP-2 (gastric adenocarcinoma cell line, diffuse type) and 1.25  $\mu$ M for ACP-03 (intestinal type) (Pinto et al. 2015). The effect of MBZ on human adrenocortical carcinoma cancer cells (H295R and SW-13) was evaluated by Martarelli et al. and the obtained results showed that MBZ significantly inhibited the in vitro growth of human adrenocortical carcinoma cells, with an  $IC_{50}$  of 0.23 and 0.27  $\mu$ M for H295R and SW-13, respectively (Martarelli et al. 2008). In addition, MBZ significantly inhibited tumor

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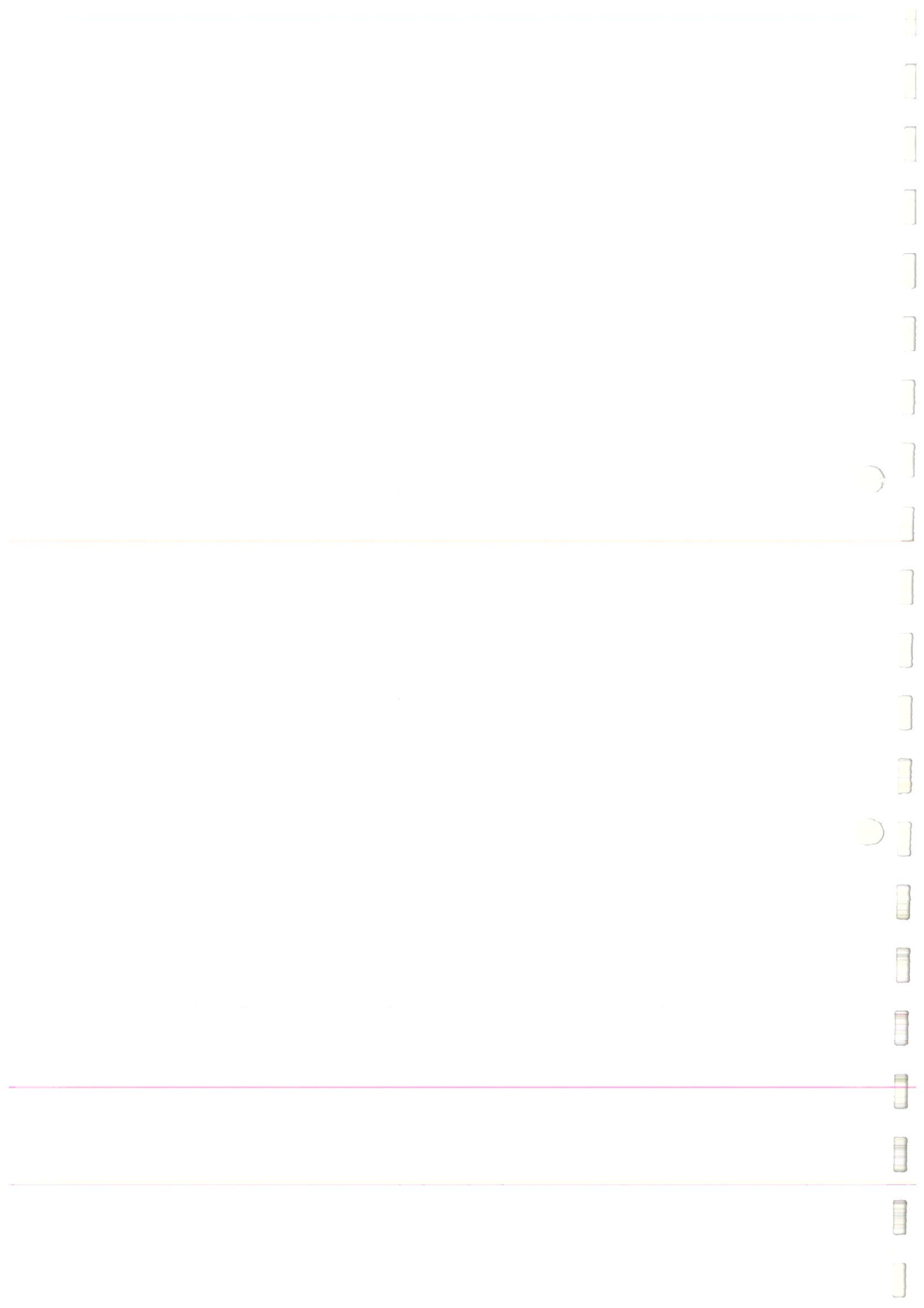




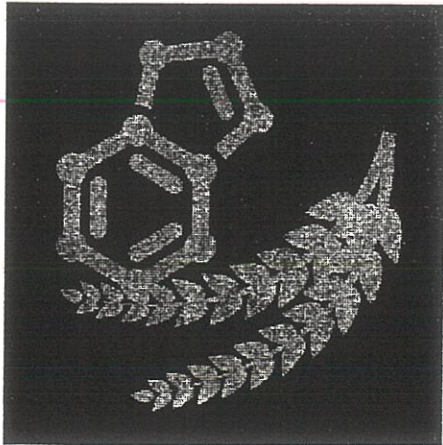
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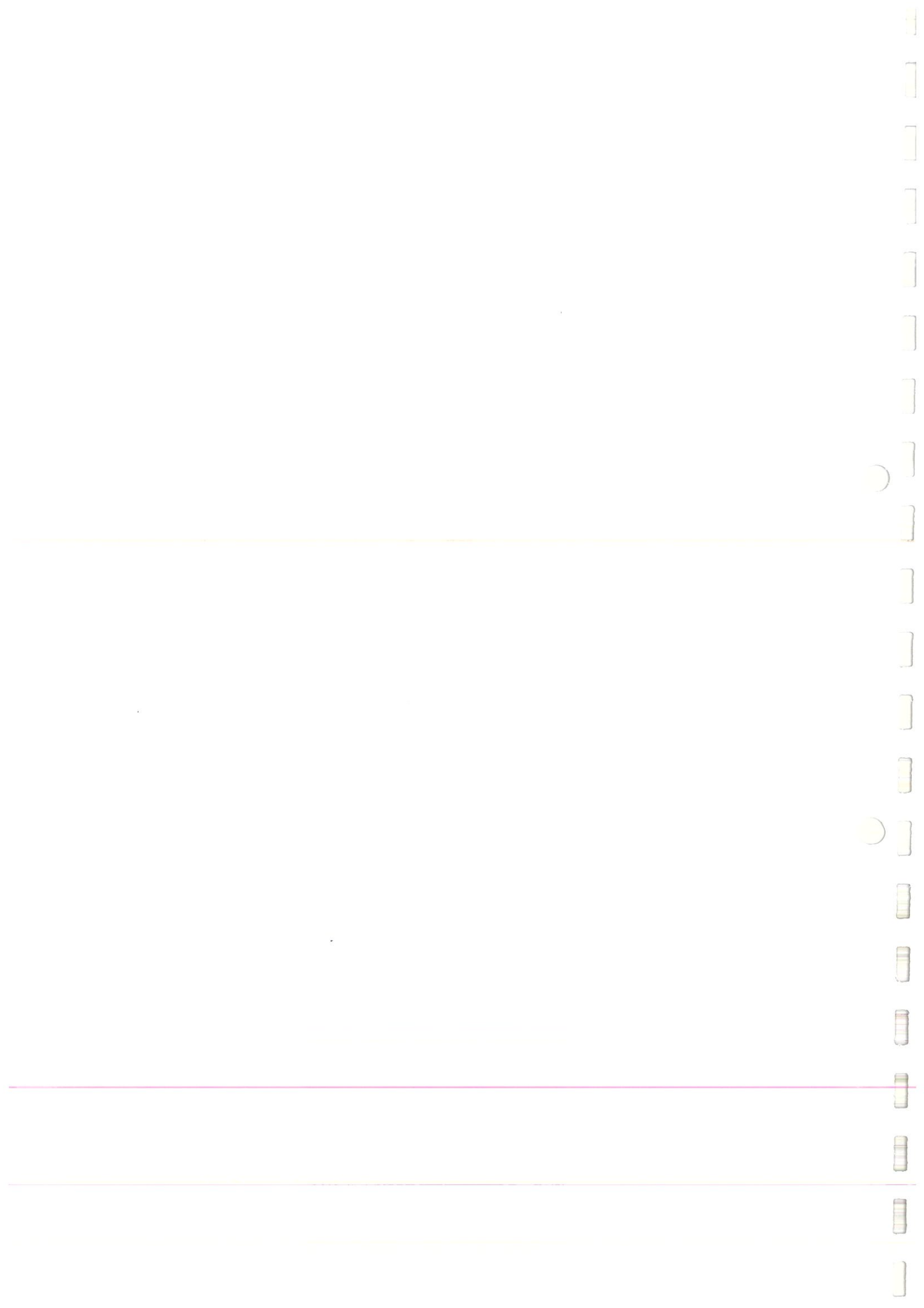
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# *nutrients*







Article

# Cinnamomum cassia and Rosa laevigata Mixture Improves Benign Prostatic Hyperplasia in Rats by Regulating Androgen Receptor Signaling and Apoptosis

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**Abstract:** Benign prostatic hyperplasia (BPH) is the most common condition in elderly men that is characterized by an increase in the size of the prostate gland. *Cinnamomum cassia* and *Rosa laevigata* have been reported to treat the symptoms associated with BPH. The aim of this study was to evaluate the effects of HT080, an herbal extract of *C. cassia* and *R. laevigata*, on a testosterone propionate (TP)-induced BPH rat model. The rats received a daily subcutaneous injection of TP (3 mg/kg) for 4 weeks to induce BPH. Rats were divided into four groups: group 1 (sham), group 2 (BPH, TP alone), group 3 (Fin, TP + finasteride 1 mg/kg/day), and group 4 (HT080, TP + HT080 200 mg/kg/day). At the end of the experiment, all rats were sacrificed, and their prostate glands were removed, weighed, and subjected to histopathological examination and western blot analyses. Serum testosterone and dihydrotestosterone (DHT) levels were determined. In addition, serum alanine and aspartate aminotransferase levels were measured to evaluate the toxicity in the liver. The Hershberger bioassay was also conducted to investigate the effects of HT080 on androgenic and antiandrogenic activities. In the BPH model, the prostate weight, prostate index, prostate epithelial thickness, and serum testosterone and DHT levels in the HT080 group were significantly reduced compared to the BPH group. Histological studies showed that HT080 reduced prostatic hyperplasia. The protein expression of androgen receptor from the HT080 group was significantly reduced in comparison with the BPH group ( $p < 0.05$ ). HT080 also induced apoptosis by regulating Bcl-2 and Bax expression. In addition, HT080 showed no toxicity in the liver and did not exhibit androgenic and antiandrogenic activities. Our finding revealed that HT080 can be a potential candidate for the treatment of BPH by regulating androgen receptor signaling and apoptosis.

**Keywords:** *Cinnamomum cassia*; *Rosa laevigata*; benign prostate hyperplasia; apoptosis; androgen receptor

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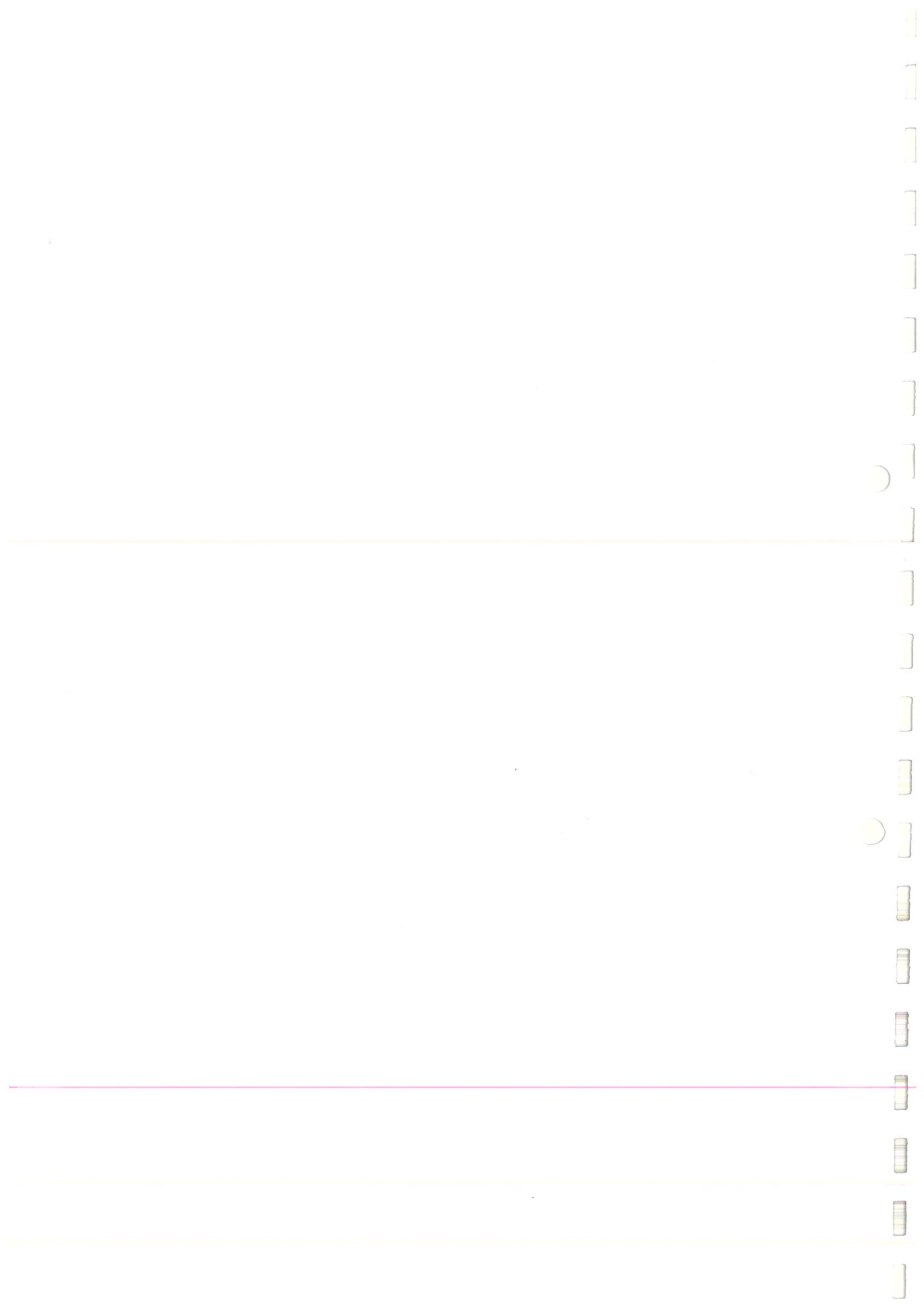
## 1. Introduction

Benign prostate hyperplasia (BPH) or prostate gland enlargement is the most common condition in middle-aged and elderly men regardless of their culture or ethnic origins [1,2]. It is characterized by an increase in the size of the prostate gland and not cancer-causing lower urinary tract symptoms (LUTSs) such as nocturia, weak urinary stream, urgency, and hesitancy [3,4]. It has been reported that the risk of BPH increases with age from 8% at age 31 to 40 years to 40–50% at age 51 to 60 years and to over 80% at age 80 years [5,6]. Much research revealed that risk factors for BPH and LUTS include hormonal alterations, obesity, diet-induced hyperinsulinemia, inflammation, lack of exercise, or glucose homeostasis as hyperglycemia [7–12]. Among them, hormonal alterations are considered the main causes of BPH, which leads to the imbalance of growth and apoptosis of prostate cells. Testosterone and dihydrotestosterone (DHT) are two main androgens that play a crucial

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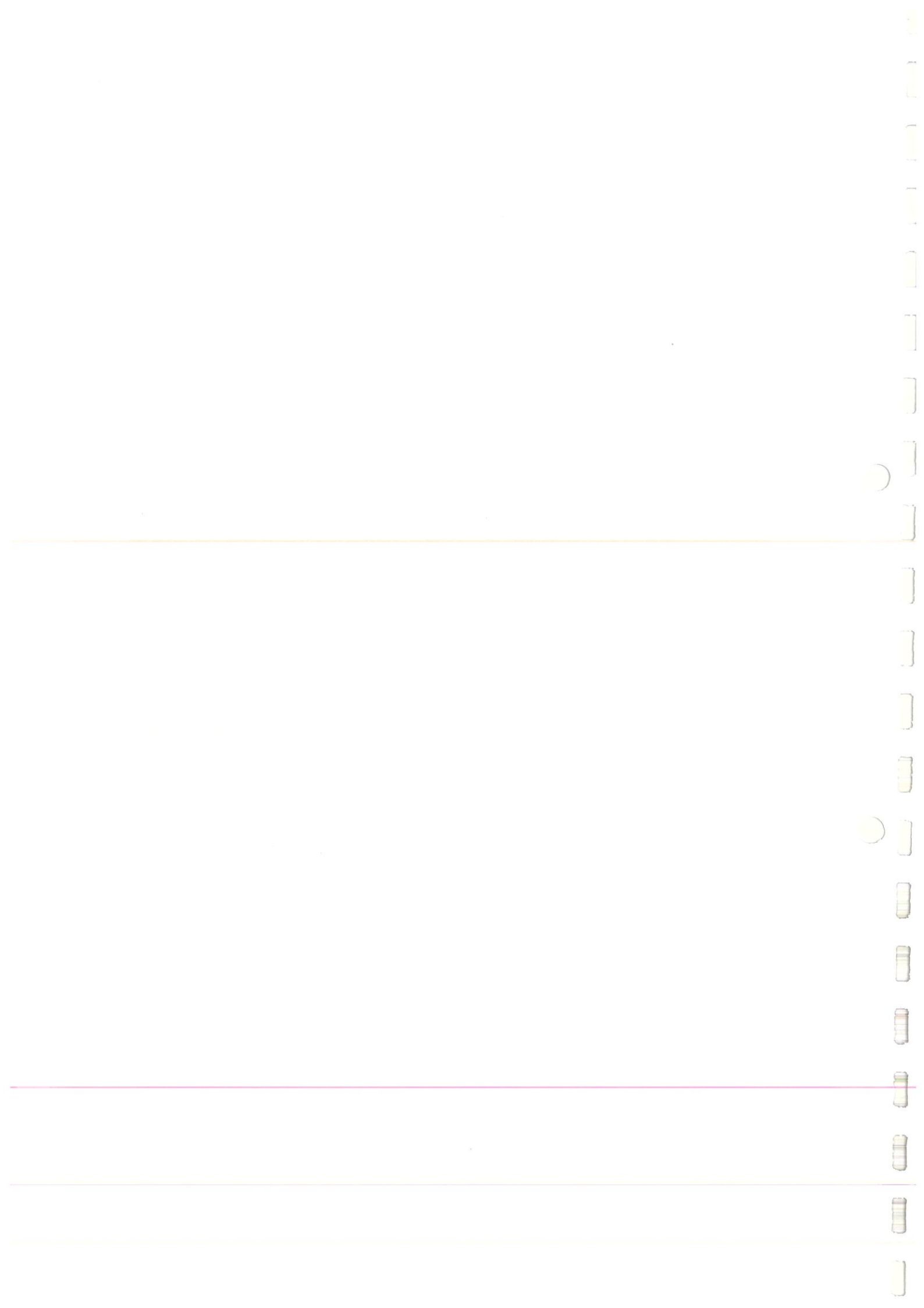
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# JDDST

Journal of Drug Delivery Science and Technology









## Co-carrier-based solid dispersion of celecoxib improves dissolution rate and oral bioavailability in rats

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### ARTICLE INFO

**Keywords:**  
Celecoxib  
Co-carrier  
Solid dispersion  
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### ABSTRACT

This study aimed to prepare a co-carrier-based solid dispersion (SD) of celecoxib (CXB) to improve its dissolution and oral bioavailability. The CXB-loaded SD formulation was prepared using CXB, pol407, Aerosil 200, and Eudragit L100 at a weight ratio of 1:3:1.5:1. PXRD, DSC, and FTIR analyses were conducted to evaluate the structural behavior and interactions between the drug and carrier. The dissolution profile was studied to demonstrate superior CXB dissolution capacity of CXB-SD than that of the physical mixture and raw CXB, and the results showed that the dissolution efficiency (%) of optimized CXB-SD significantly ( $P < 0.05$ ) increased compared to that of raw CXB. The mean dissolution times of CXB-SD at pH 1.2 and 6.8 were reduced by 2.4-fold and 2.5-fold, respectively, compared to that of raw CXB. The dissolution of CXB-SD fitted well with the zero-order model. The preparation of the CXB-SD formulation improved the bioavailability of CXB, as demonstrated by the increased  $AUC_{0-8h}$  (1.88-fold) and  $C_{max}$  (2.24-fold) of CXB-SD compared to that of raw CXB. In conclusion, these results indicate that SDs can enhance the dissolution and oral bioavailability of poorly water-soluble CXB.

### 1. Introduction

Celecoxib (CXB; 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-pyrazol-1-yl]-benzenesulfonamide), a nonsteroidal anti-inflammatory drug belonging to the class of selective cyclooxygenase-2 inhibitors, is used in the treatment of osteoarthritis, rheumatoid arthritis, and acute pain [1, 2]. However, due to poor aqueous solubility (1–3  $\mu\text{g}/\text{mL}$ ) [3], CXB is categorized as a biopharmaceutics classification system (BCS) class II drug. Drug solubility is the major factor affecting the oral absorption of BCS class II drugs from the gastrointestinal tract [4,5]. In particular, the oral bioavailability of CXB is low, varying from 22% to 40% [6]. Therefore, improving the solubility of CXB may enhance its dissolution rate and bioavailability [7].

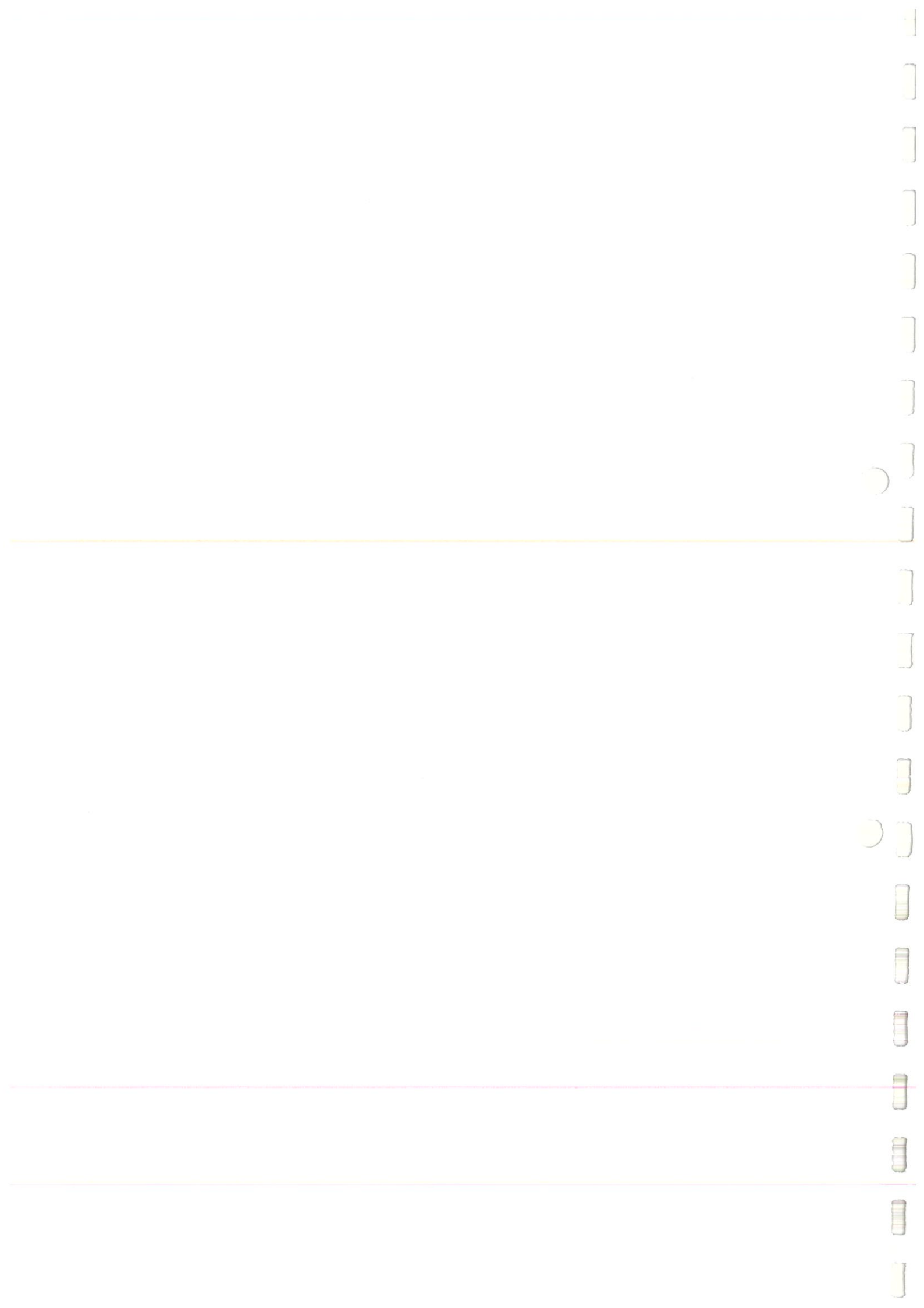
Solid dispersion (SD) is a simple and effective technique in the pharmaceutical industry to improve the solubility of poorly water-soluble drugs [4,8,9]. SDs are systems in which hydrophobic drugs are dispersed molecularly in one or more hydrophilic carriers to reduce particle size, increase surface area, improve wettability, and transform the crystalline state of a drug into an amorphous state [10,11]. This was first introduced by Sekiguchi and Obi, using urea as a carrier for

sulfathiazole-SD formulation [12]. With the development of science and technology in the pharmaceutical industry, various carriers used in the preparation of SDs, including acids, sugars, soluble polymers, insoluble polymers, surfactants, inert carriers, and miscellaneous, have been reported in the literatures [13]. Owing to the increased solubility of CXB, CXB-SDs with various carriers (Soluplus, Poloxamer 188, Poloxamer 407, polyethylene glycol (PEG), polyvinyl alcohol (PVA), hydropropyl methylcellulose (HPMC), polyvinylpyrrolidone (PVP), and Eudragit®) have been formulated in several studies with many interesting results. A binary SD system of CXB and a carrier was successfully prepared with poloxamer 407, PVP, HPMC, and PEG, which increased the solubility of CXB 65, 31, 38, and 23.5 times that of raw CXB, respectively [14]. Jeon et al. prepared a ternary system of CXB-SD with PVP-K30 or Eudragit EPO as aqueous carriers and poloxamer 407 as a surfactant using the spray drying method [15]. The obtained data showed that the CXB-SD formulations increased the dissolution of CXB. When PVP-K30 was used as the carrier, the dissolution rate increased with increasing PVP concentration, and CXB was released gradually in CXB-PVPK30-SDs. The use of Eudragit EPO as a carrier showed fast and complete release of CXB and no difference in the dissolution profiles of CXB-Eudragit

<sup>\*</sup> Corresponding author

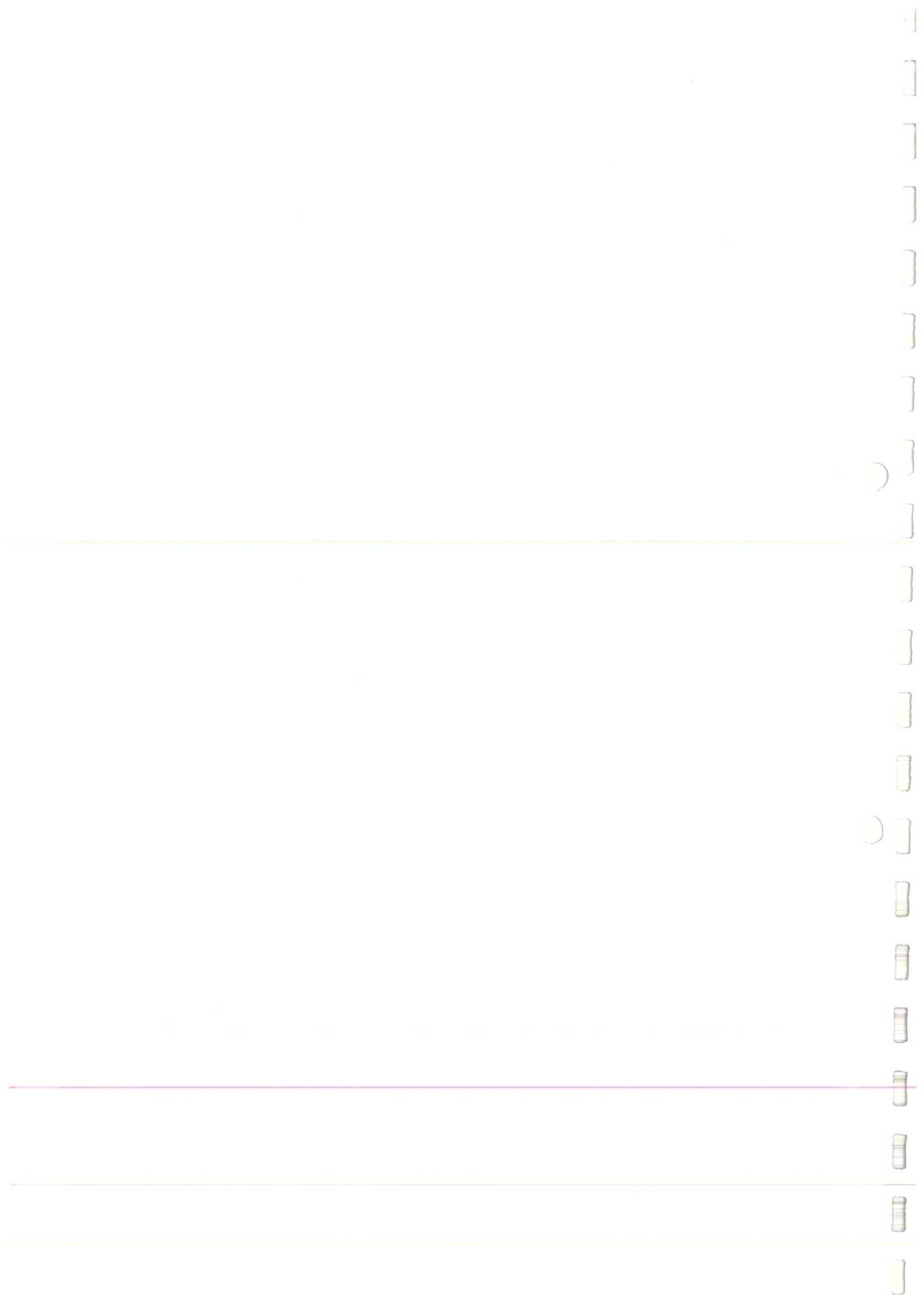
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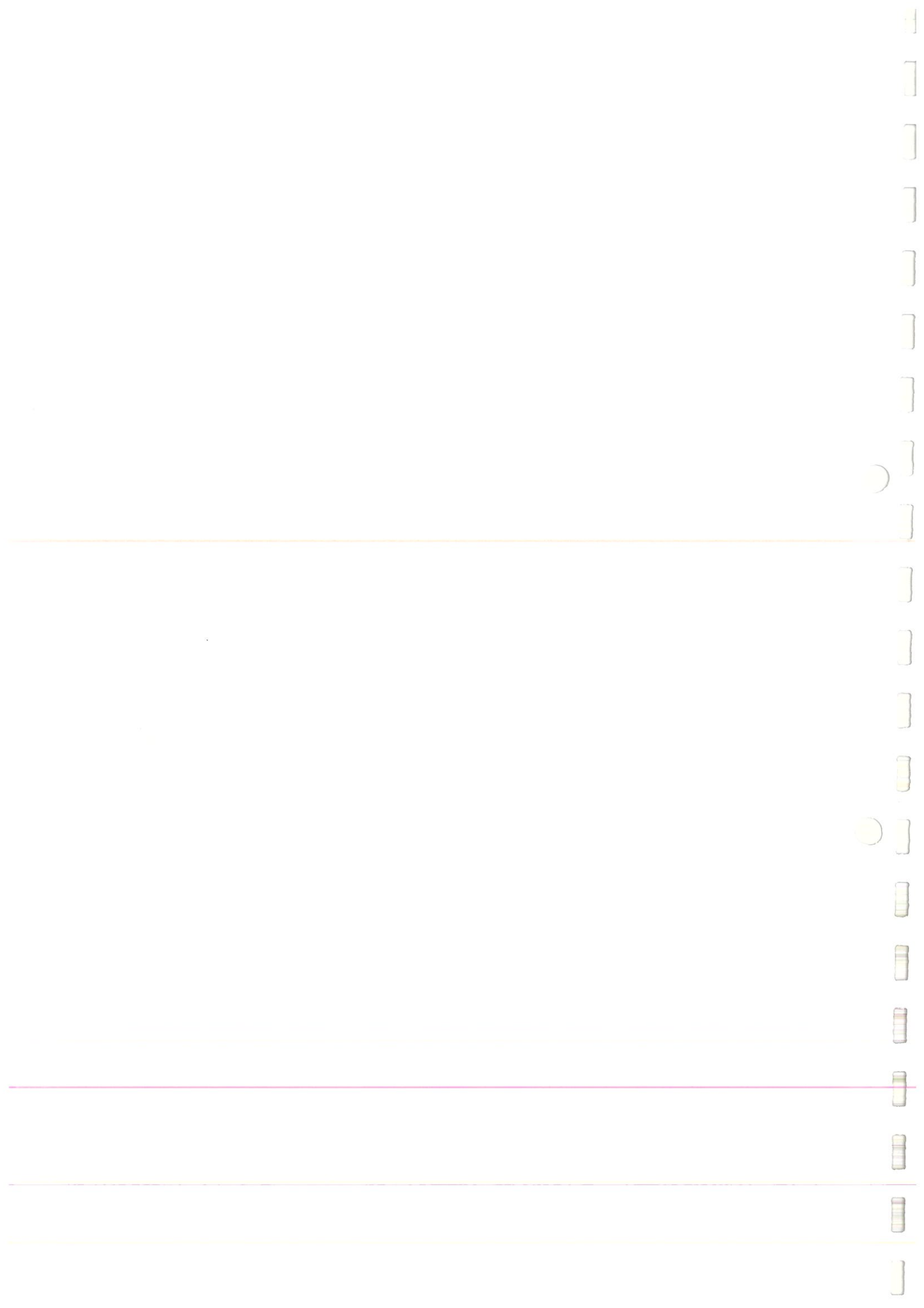
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# Alginate-coated chitosan nanoparticles protect protein drugs from acid degradation in gastric media

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## Abstract

**Purpose** The aim of this study was to design and evaluate chitosan nanoparticles (CS NPs) coated with alginate which protect protein drugs from acid degradation. The model protein drug used was bovine serum albumin (BSA).

**Methods** BSA-loaded CS NPs (BSA-CS NPs) were prepared using the ionic gelation method with sodium tripolyphosphate and the surface of the BSA-CS NPs were coated with sodium alginate (Alg). The optimized alginate-coated BSA-CS NPs (Alg-BSA-CS NPs) were evaluated for BSA degradation in an acidic medium.

**Results** The encapsulation efficiency (EE), particle size, polydispersity index, and zeta potential of the prepared Alg-BSA-CS NPs were 95.2%, 476.4 nm, 0.24, and  $-53.8$  mV, respectively. An *in vitro* release study showed that the initial burst release of BSA from the BSA-CS NPs was higher than that from the Alg-BSA-CS NPs. Cytotoxicity analysis revealed that the Alg-BSA-CS NPs were non-toxic to Caco-2 cells. The *in vitro* cellular uptake of the Alg-BSA-CS NPs in Caco-2 cells was significantly higher than that of the BSA-CS NPs and free BSA. Sodium dodecyl sulfate–polyacrylamide gel electrophoresis showed that the Alg-BSA-CS NPs protected BSA from degradation in an acidic environment.

**Conclusion** Alg-BSA-CS NPs are suitable for the oral delivery of protein drugs by preventing protein degradation in acidic environments.

**Keywords** Protein protection · Acid degradation · Nanoparticles · Chitosan · Alginate · Oral delivery

## Introduction

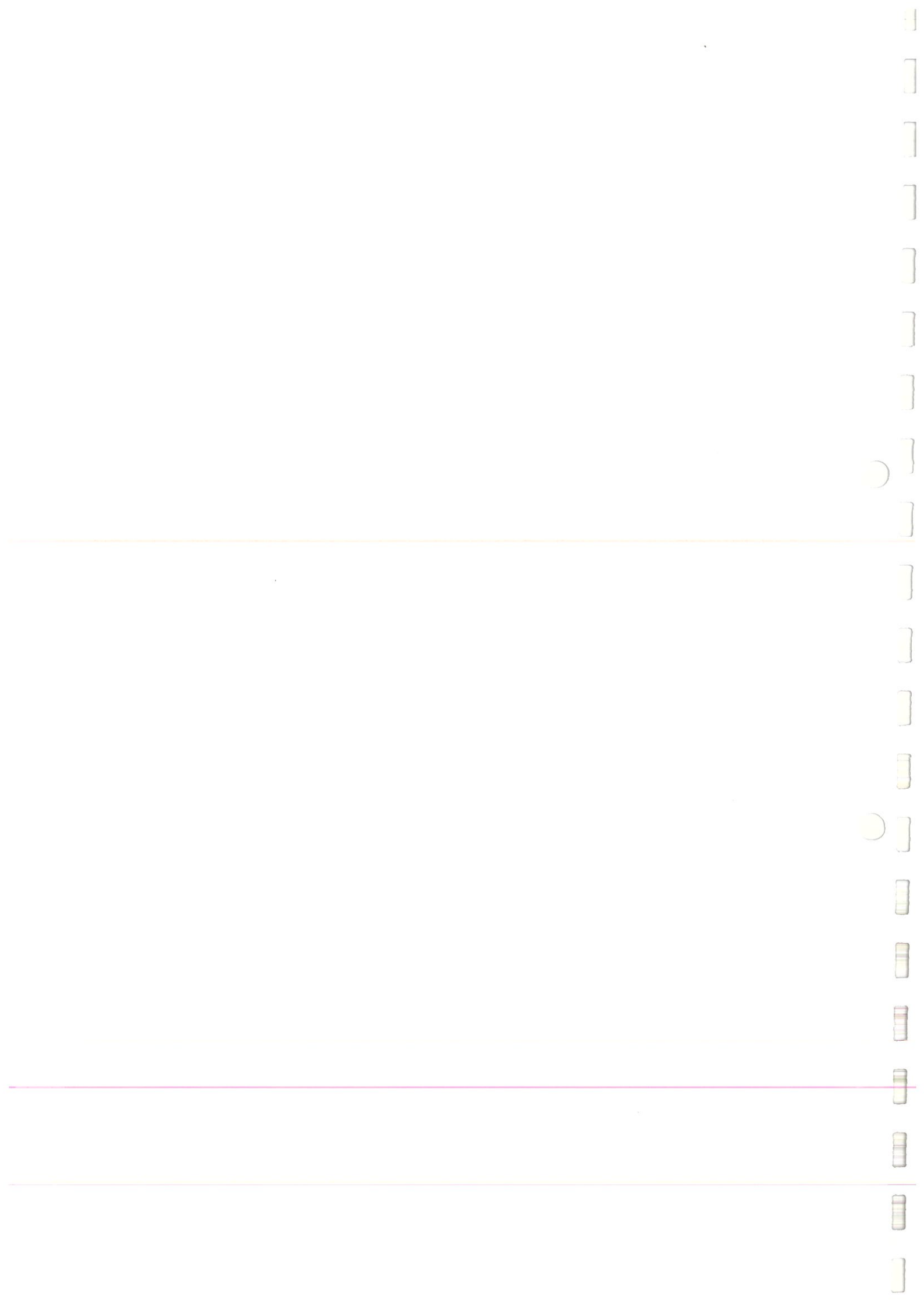
With advances in biotechnology in recent years, protein drugs have received increasing attention for the treatment of various diseases owing to their high potency and low toxicity (Frokjaer and Otzen 2005). Oral administration is the preferred route of drug delivery. However, the absorption of protein drugs from the gastrointestinal (GI) tract is usually hampered by instability and degradation caused by stomach acids, resulting in decreased drug efficacy and poor bioavailability. Therefore, the development of novel protein drug formulations to overcome these problems is an important research subject in the pharmaceutical industry (Torchilin and Lukyanov 2003; Al-Tahami and Singh 2007). Various strategies have been developed to overcome these problems, such as the use of microparticles and nanoparticles (NPs) (Su

et al. 2012; Jain et al. 2012; Muheem et al. 2016), liposomes (Okada et al. 1997; Kurz and Ciulla 2002; Mohanraj et al. 2010), micro/nanoemulsions (Mueller et al. 1994; Park et al. 2011; Patil et al. 2019), and solid core particles (Müller et al. 2000; Sarmiento et al. 2007). Among these, nanoparticles (NPs) have recently received considerable attention. NPs prepared for protein drugs typically use carriers, such as gelatin, starch, or chitosan (CS), for the controlled release of protein drugs (Ghormade et al. 2011).

In this study, CS, a polysaccharide derived from chitin, was used to prepare NPs. CS is a potent natural polymer consisting of  $\beta$ -(1–4)-linked d-glucosamine (deacetylated units) and N-acetyl-d-glucosamine (acetylated units) (Sinha et al. 2004; Wang et al. 2005; Amidi et al. 2010; Kumari et al. 2010). It is insoluble in water but soluble in acidic solutions. Additionally, it provides many advantages as a carrier for NPs, such as biodegradability, biocompatibility, mucoadhesiveness, and low toxicity (Shu and Zhu 2002; Sinha et al. 2004; Amidi et al. 2010). However, the CS formulation can be deprotonated in a physiological environment, causing it to lose its mucoadhesive properties and permeation-enhancing

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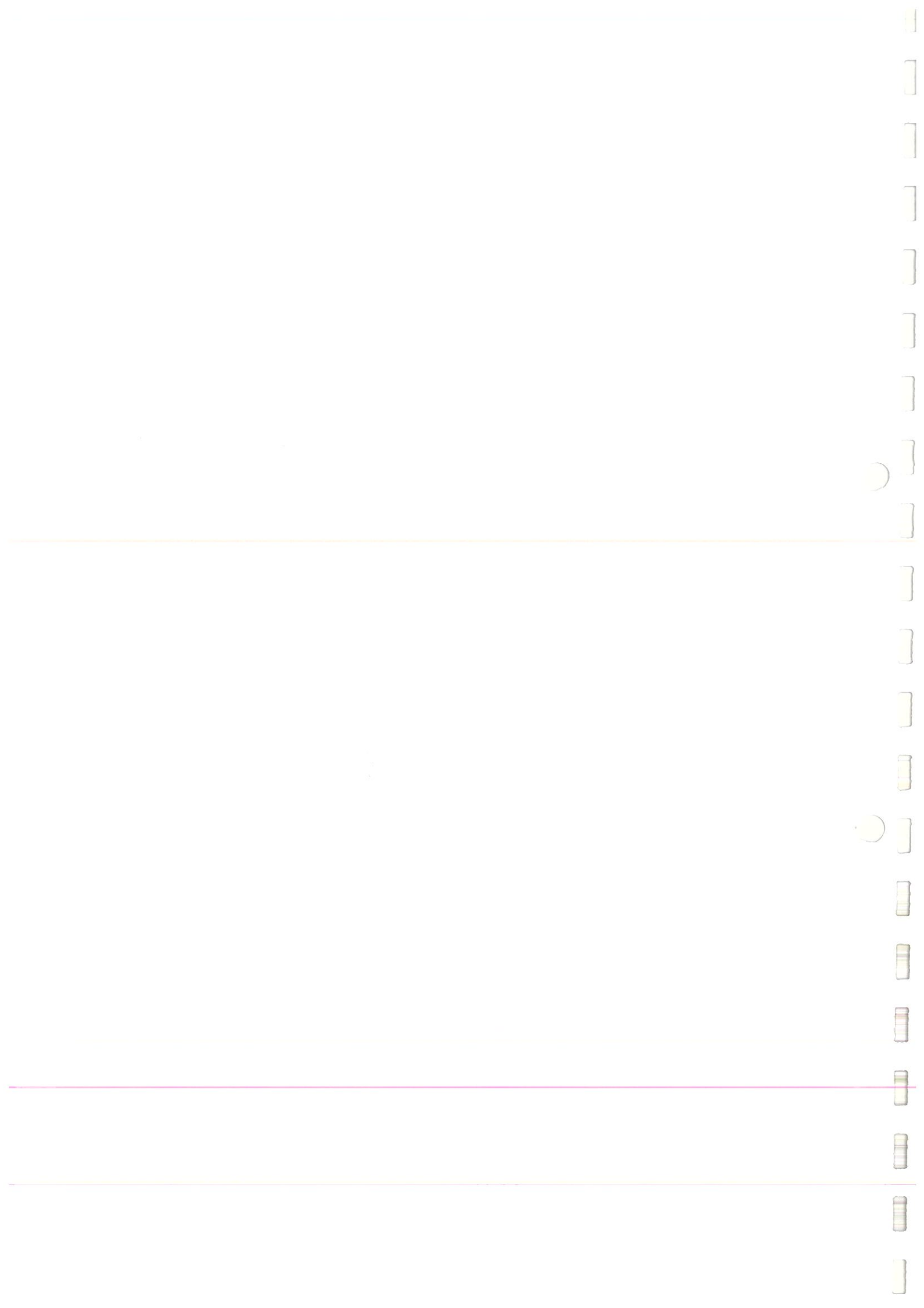
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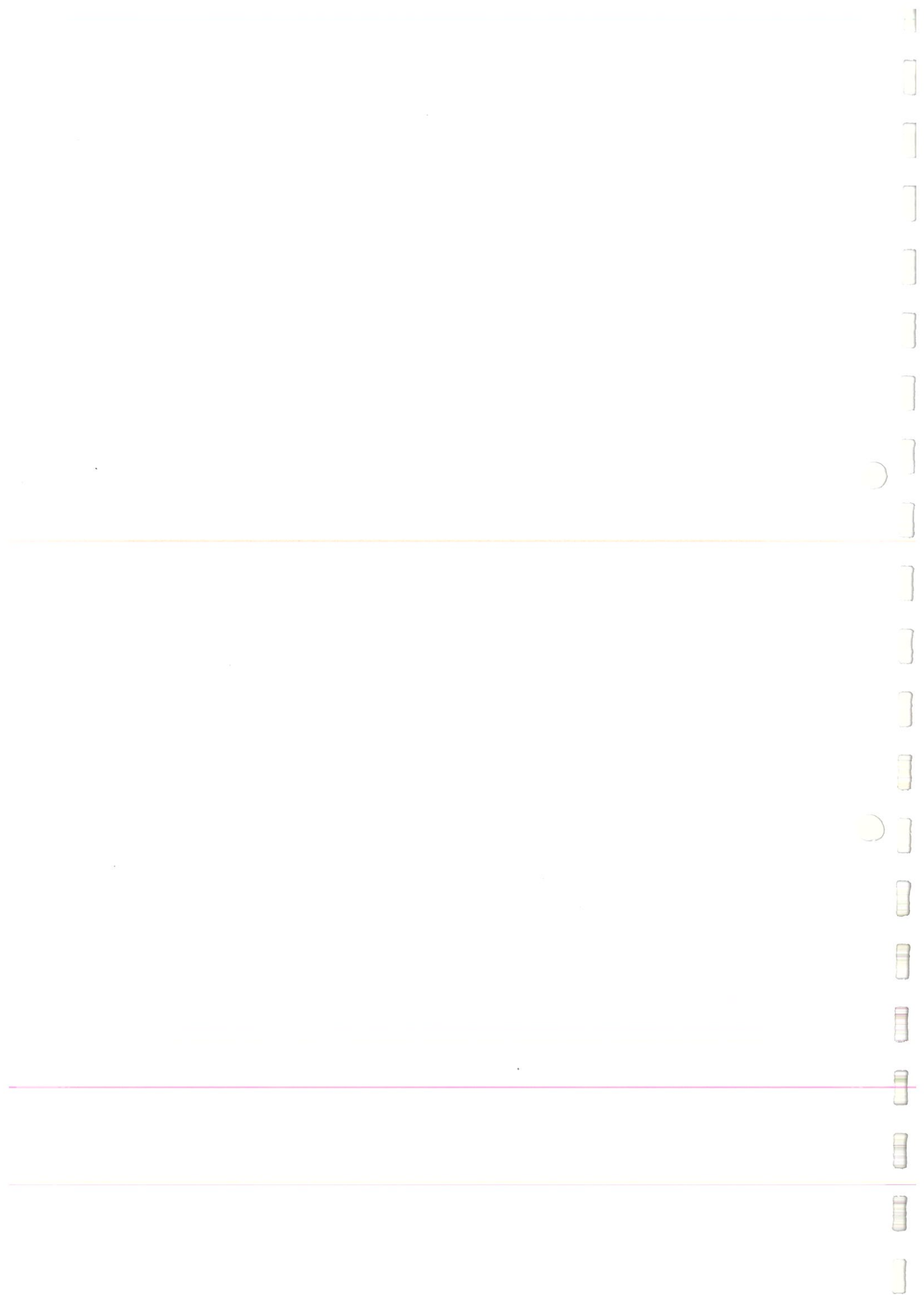




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# Application of supercritical fluid technology for solid dispersion to enhance solubility and bioavailability of poorly water-soluble drugs

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## ABSTRACT

Many new chemical entities (NCEs) have been discovered with the development of the pharmaceutical industry. However, the main disadvantage of these drugs is their low aqueous solubility, which results in poor bioavailability, posing a challenge for pharmaceutical scientists in the field of drug development. Solid dispersion (SD) technology is one of the most successful techniques used to resolve these problems. SD has been widely used to improve the solubility and bioavailability of poorly water-soluble drugs using several methods such as melting, supercritical fluid (SCF), solvent evaporation, spray drying, hot-melt extrusion, and freeze-drying. Among them, SCF with carbon dioxide (CO<sub>2</sub>) has recently attracted great attention owing to its enhanced dissolution and bioavailability with non-toxic, economical, non-polluting, and high-efficiency properties. Compared with the conventional methods using organic solvents in the preparation of the formulation (solvent evaporation method), SCF used CO<sub>2</sub> to replace the organic solvent with high pressure to avoid the limitation of solvent residues. The solubility of a substance in CO<sub>2</sub> plays an important role in the success of the formulation. In the present review, the various processes involved in SCF technology, application of SCF to prepare SD, and future perspectives of SCF are described.

## 1. Introduction

Improvements in solubility and oral bioavailability (BA) of drugs with poor aqueous solubility drugs play an important role in drug development (Ha et al., 2020; Kim et al., 2020, 2021; Tran and Park, 2021). The oral route of administration is preferred over other routes (intravenous, intramuscular, and subcutaneous), owing to several advantages such as safety, pain avoidance, and good patient compliance. After ingestion via the oral route, the drugs must dissolve in the gastrointestinal (GI) fluid to enable their penetration into the bloodstream through the GI tract membrane. Absorption is affected by many factors, such as blood perfusion, differences in luminal pH along the GI tract, the presence of bile and mucus, surface area per luminal volume, and the nature of epithelial membranes. Drugs belonging to the biopharmaceutical classification system (BCS) class II exhibit poor aqueous solubility, indicating dissolution rate-limited absorption, resulting in poor BA.

Solid dispersion (SD) is a promising technique for improving the aqueous solubility and BA of BCS class II drugs by enhancing wettability, reducing particle size, high porosity, and the amorphous state (Byeon

et al., 2019; Kim et al., 2021; Luu et al., 2019; Tran et al., 2019). It is simpler and easier to prepare than other methods such as lipid-based systems (Chen et al. 2018a, 2018b; Kim et al., 2017), micronization (Aguilar et al., 2018; Karashima et al., 2017; Seo et al., 2016), co-crystals (Reggane et al., 2018), and nanonization (Chen et al. 2018a, 2018b; Park et al., 2018; Wong et al., 2018). SD is defined as the dispersion of a hydrophobic drug in hydrophilic carriers to improve its surface area or change the state of the drug (crystalline to amorphous). With the recent development of the pharmaceutical industry, products with minimal environmental impact and less toxicity have become more attractive. Therefore, technological development is the top priority. In this regard, high-pressure technology is currently receiving great attention, and supercritical fluids (SCFs) are still popular in this area. Unlike other methods [fusion method (Karolewicz et al., 2016), solvent evaporation method (Mustapha et al., 2017), lyophilization technique (Kaur et al., 2017), or spray drying method (Pradhan et al., 2015)], SCF can be used to prepare amorphous SD with many advantages such as controllable processing conditions, good reproducibility, and environmental friendliness (Han et al., 2019). SCF was introduced in the late 1980s and the early 1990s. In 1879, Hannay and Hogarth (1879) reported an SCF for

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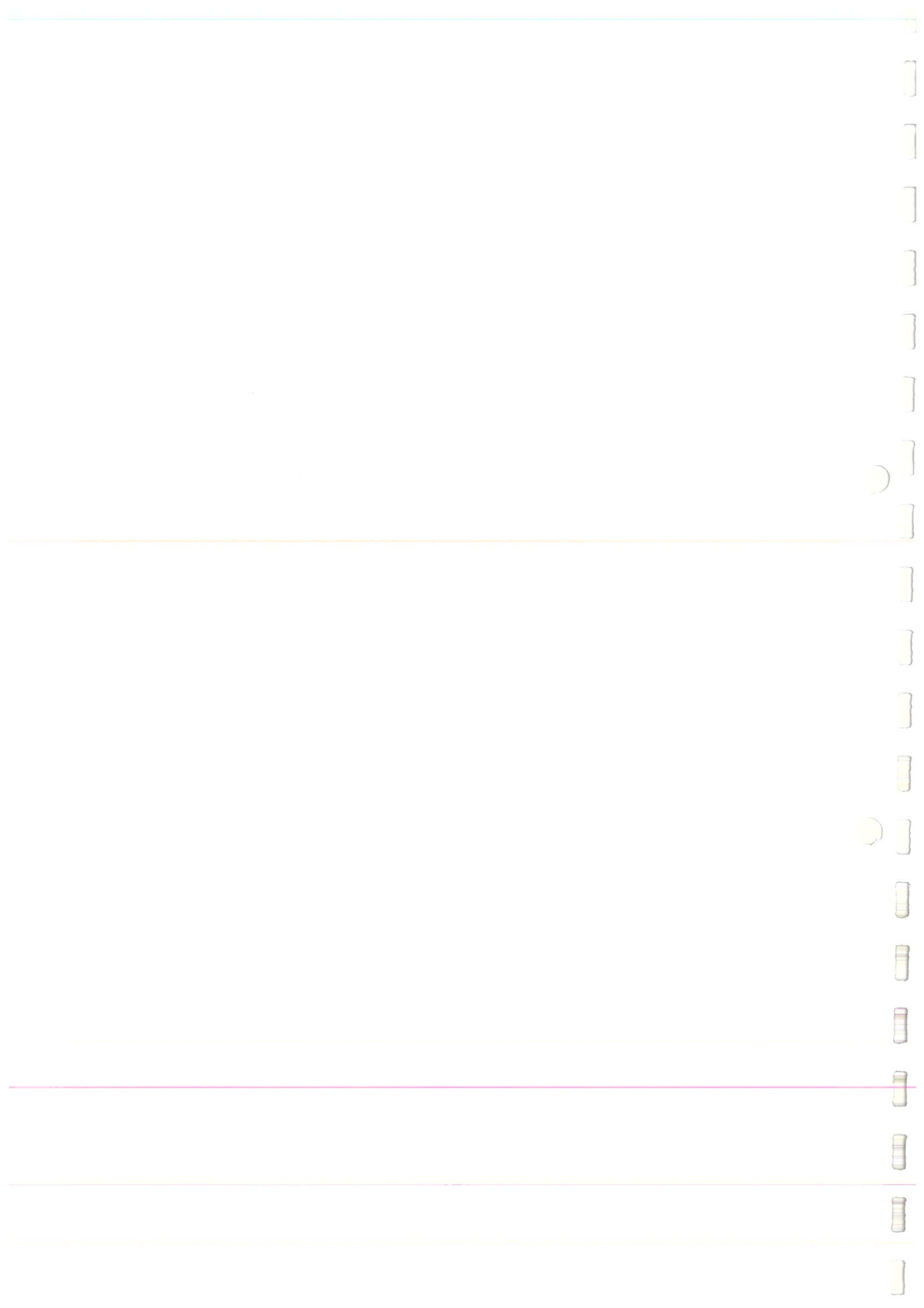
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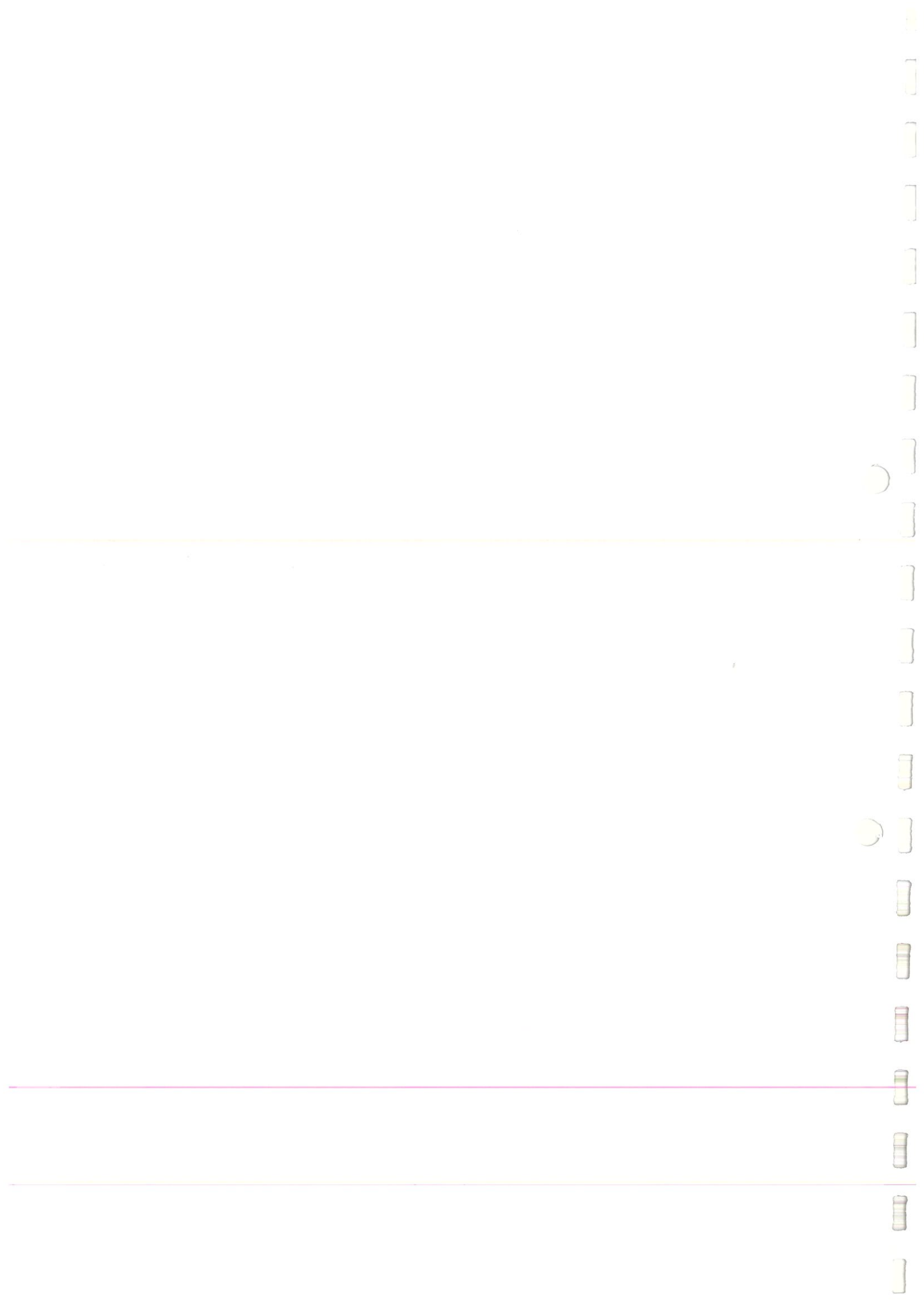
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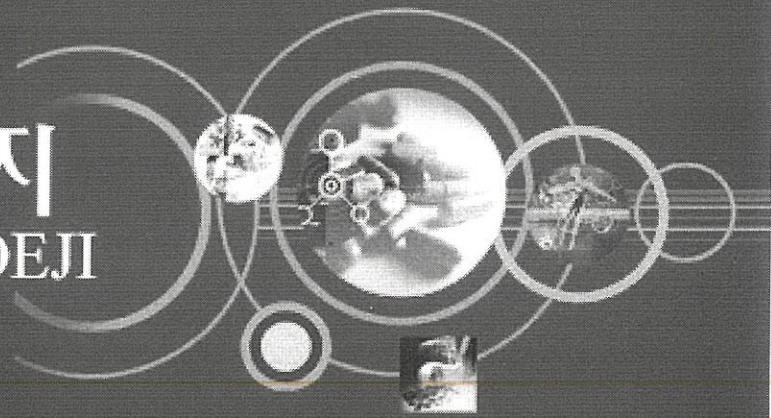


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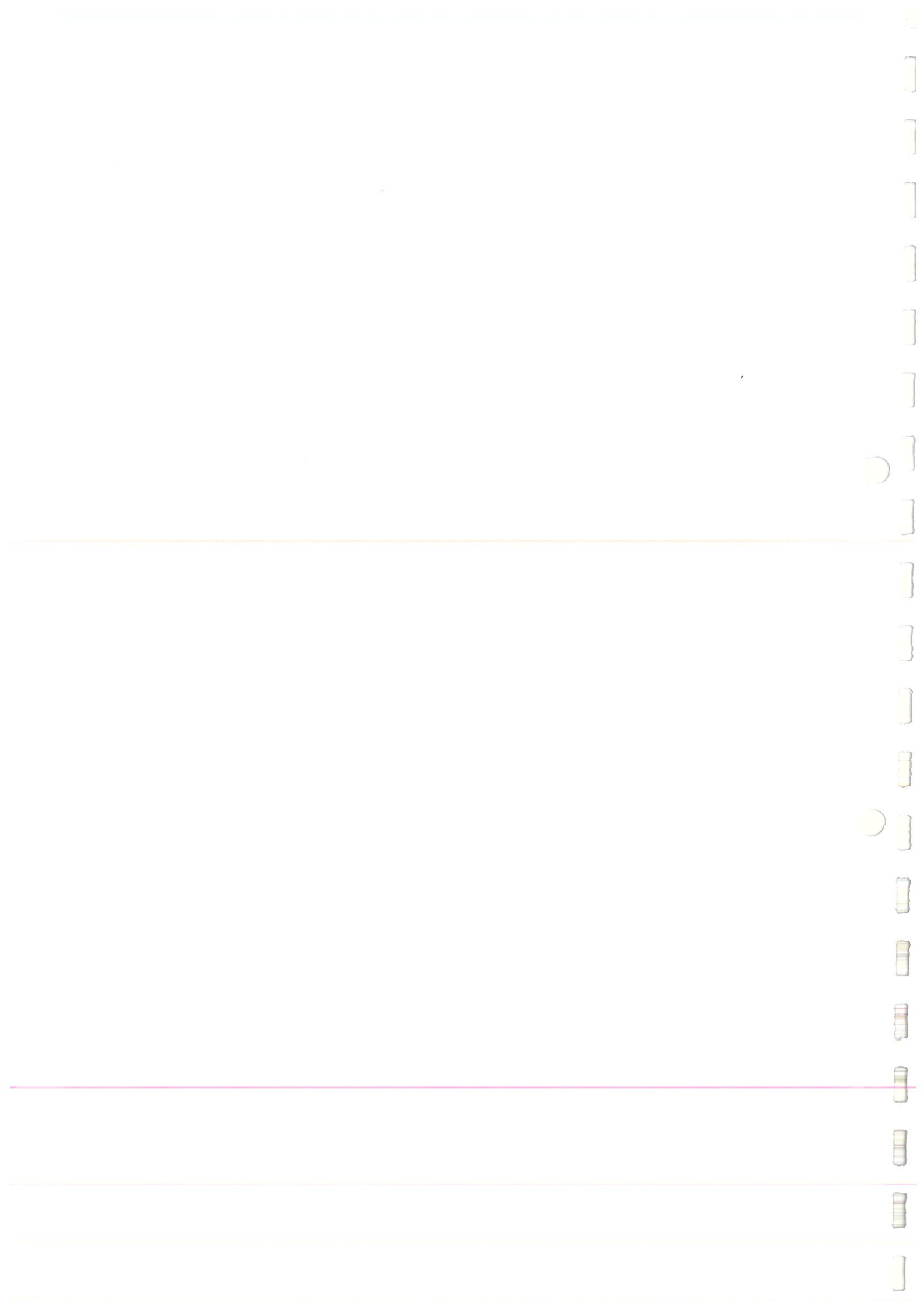


약학회지  
YAKHAK HOEJI











## Local drug delivery using poly(lactic-co-glycolic acid) nanoparticles in thermosensitive gels for inner ear disease treatment

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### ABSTRACT

Intratympanic (IT) therapies have been explored to address several side effects that could be caused by systemic administration of steroids to treat inner ear diseases. For effective drug delivery to the inner ear, an IT delivery system was developed using poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) and thermosensitive gels to maintain sustained release. Dexamethasone (DEX) was used as a model drug. The size and zeta potential of PLGA NPs and the gelation time of the thermosensitive gel were measured. *In vitro* drug release was studied using a Franz diffusion cell. Cytotoxicity of the formulations was investigated using SK-MEL-31 cells. Inflammatory responses were evaluated by histological observation of spiral ganglion cells and stria vascularis in the mouse cochlea 24 h after IT administration. In addition, the biodistribution of the formulations in mouse ears was observed by fluorescence imaging using coumarin-6. DEX-NPs showed a particle size of  $150.0 \pm 3.2$  nm in diameter and a zeta potential of  $-18.7 \pm 0.6$ . The DEX-NP-gel showed a gelation time of approximately 64 s at 37 °C and presented a similar release profile and cytotoxicity as that for DEX-NP. Furthermore, no significant inflammatory response was observed after IT administration. Fluorescence imaging results suggested that DEX-NP-gel sustained release compared to the other formulations. In conclusion, the PLGA NP-loaded thermosensitive gel may be a potential drug delivery system for the inner ear.

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Inner ear drug delivery; intratympanic administration; thermosensitive gel; PLGA nanoparticles; dexamethasone


### 1. Introduction

Hearing loss caused by inner ear disease is increasing because of prolonged exposure to noise, increased life expectancy, and the use of medicines such as anticancer drugs (Kim, 2017). Therefore, there is a growing interest in drug delivery to the inner ear. Glucocorticoid drugs, such as dexamethasone (DEX), are considered potential otoprotective drugs with anti-inflammatory effects (Van De Water et al., 2010). However, systemic drug administration usually results in only a small amount of drug that reaches the inner ear and a risk of side effects. The benefits of inner ear drug delivery are that they do not cross the blood-labyrinth barrier, avoid first-pass metabolism from systemic administration, maintain high drug concentrations in the inner ear, and reduce the total amount of administered drug (Juhn et al., 1982; Mäder et al., 2018).

Intratympanic (IT) administration, a process in which drugs are injected into the middle ear through the eardrum to

deliver drugs into the inner ear, has been studied for many years (Ersner et al., 1951; Schuknecht, 1956). Since the mid-1990s, local drug delivery to the ear has been used as a clinical treatment. If the drug is administered to the middle ear, it must pass through the round window membrane (RWM) to reach the inner ear (Nedzelski et al., 1993; Toth & Parnes, 1995). Therefore, the administered drug must remain in the middle ear for sufficient time and be in contact with the RWM. However, the drug administered to the middle ear is rapidly removed into the Eustachian tube through the flow of the mucosa (Salt & Plontke, 2018).

Over the past several years, biodegradable polymer nanoparticles (NPs) have attracted interest for drug delivery to the inner ear. As a carrier for local drug administration, NPs composed of poly(lactic-co-glycolic acid) (PLGA), approved by the Food and Drug Administration and the European Medicine Agency, have been considered an ideal carrier (Blasi, 2019; Elmowafy et al., 2019; Schoubben et al., 2019). Previous studies have demonstrated the application of

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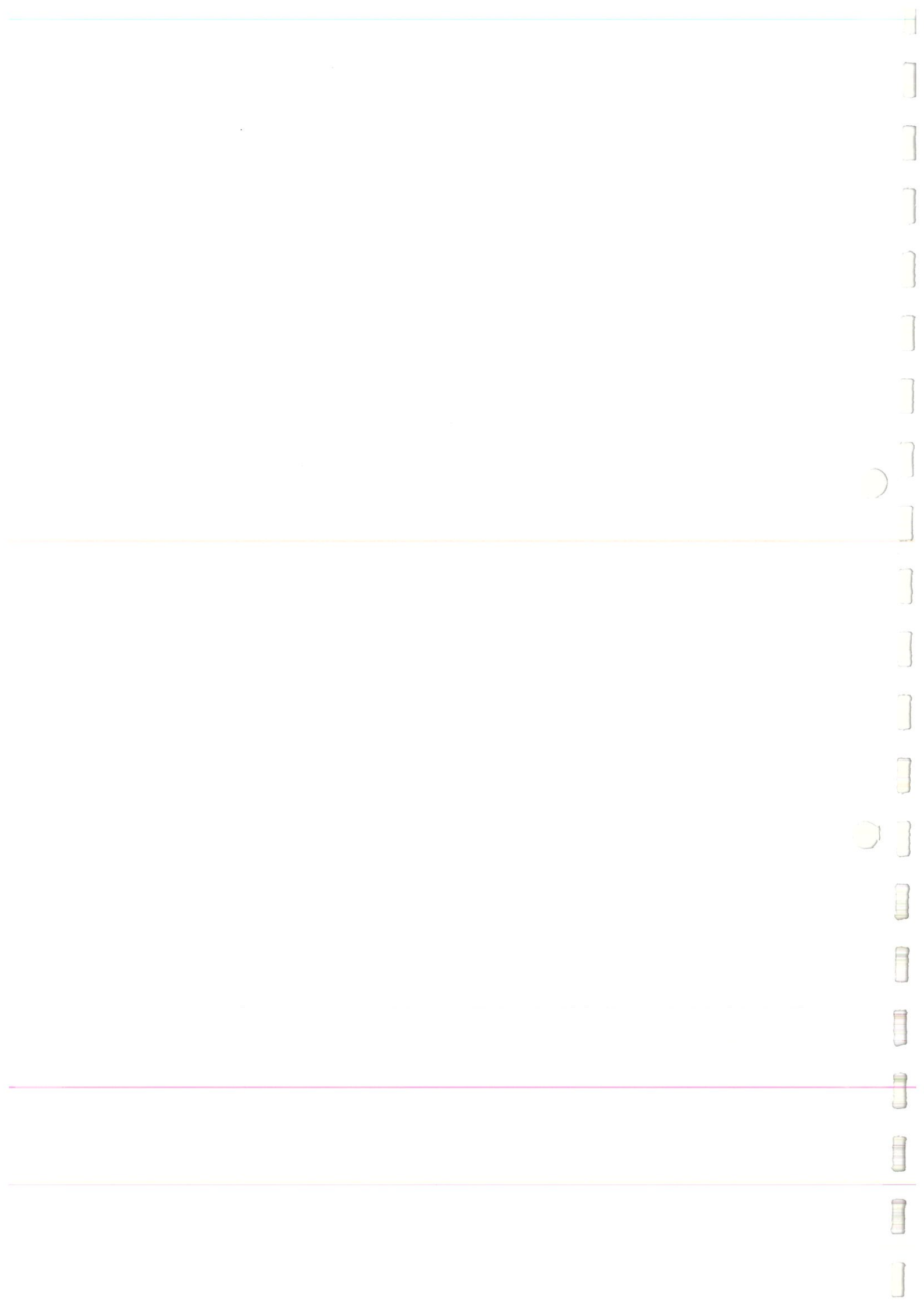
\*Both authors contributed equally to this work.

Dong-Hyun Kim, Thu Nhan Nguyen, Phuong Tran: performed experiments, conceptualization, investigation, writing – original draft. Thu Nhan Nguyen: performed data analysis, revision, and discussion. Dong-Hyun Kim, Phuong Tran, Jinhyung Rho: performed investigation on animal study. Young-Min Han: performed experiments. Jae-Young Lee, Hwa-Young Son, Jeong-Sook Park: performed data analysis, review, and discussion. Jeong-Sook Park: performed writing and editing, supervision, revision.

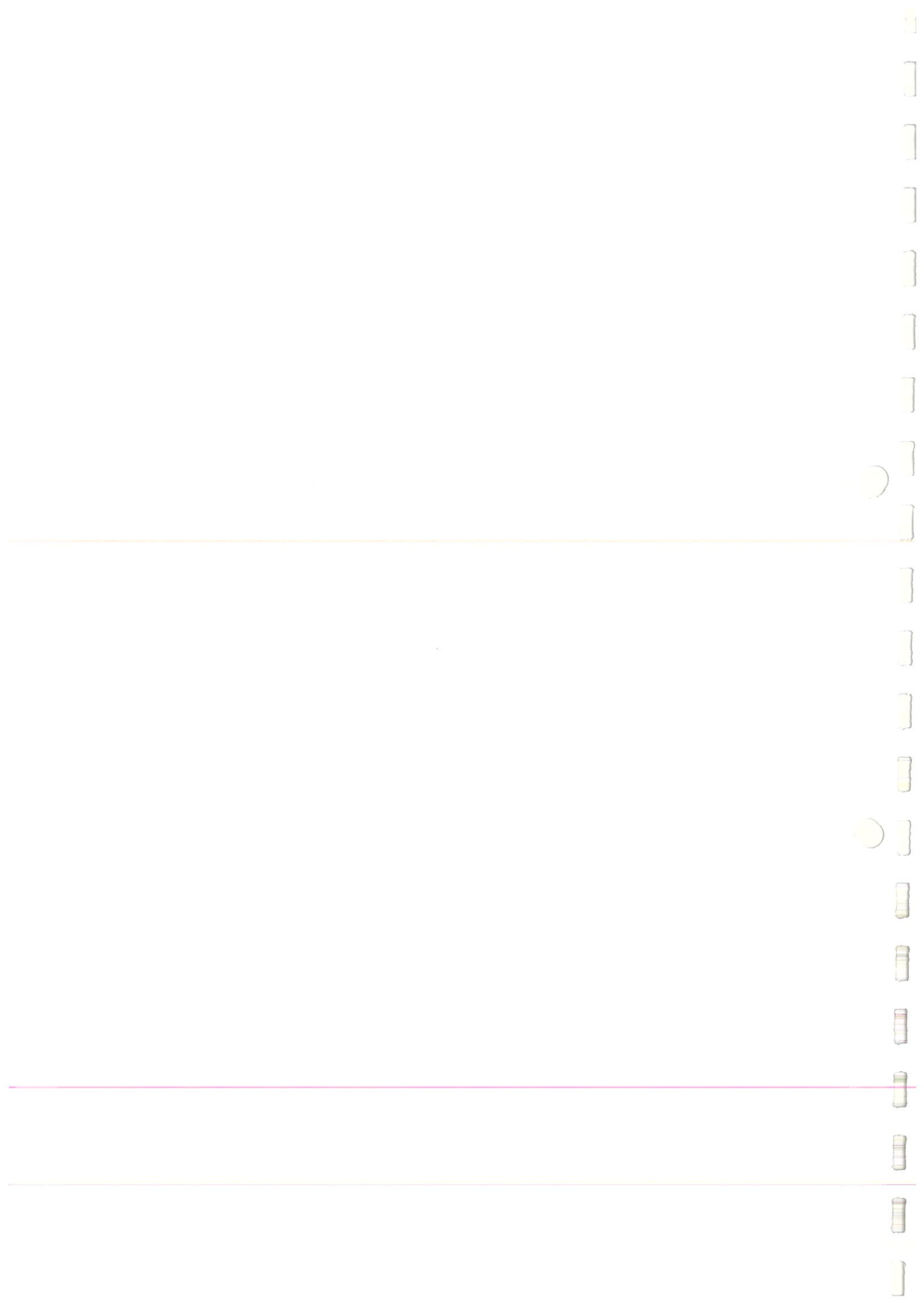
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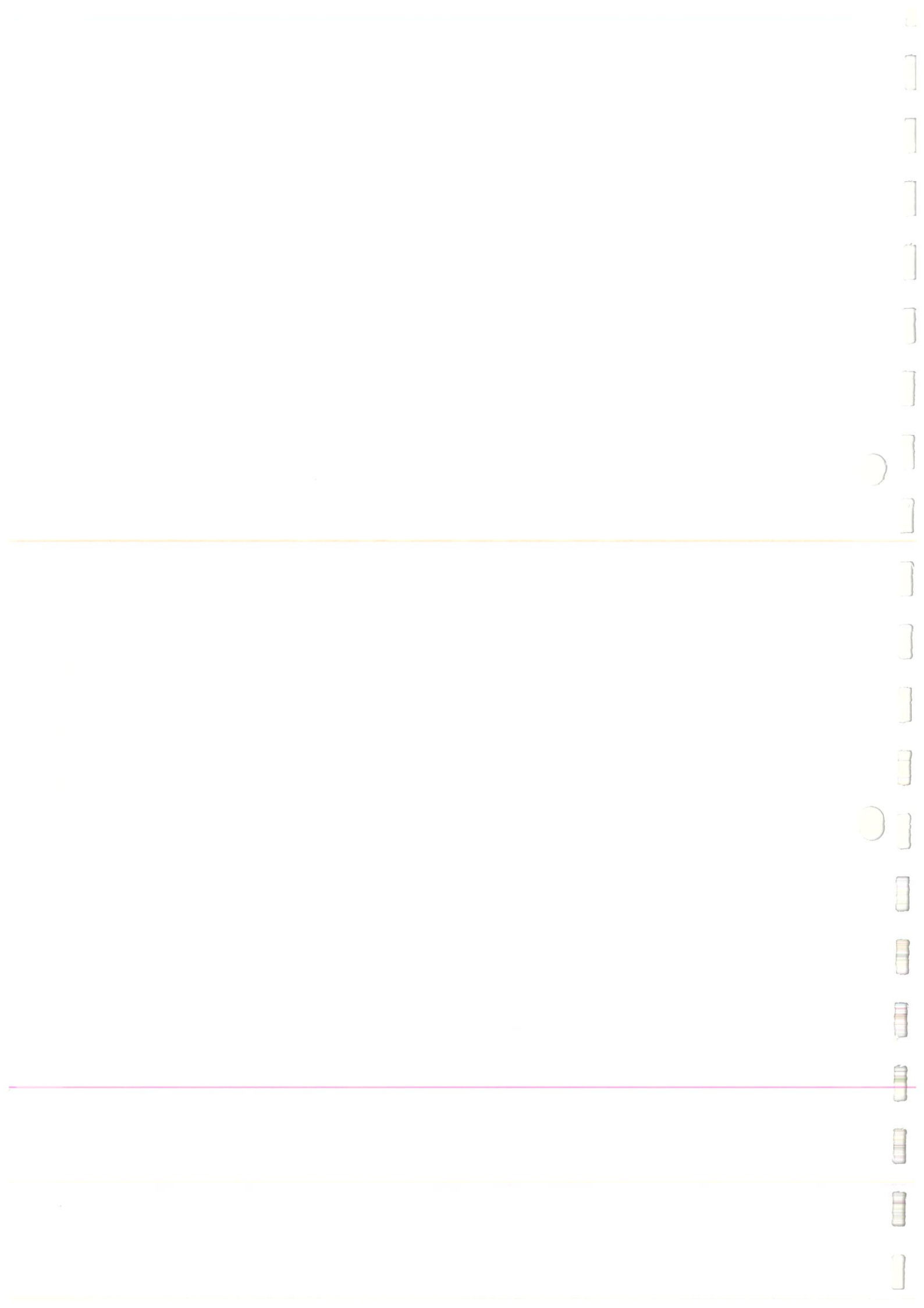
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Original Article

## Docetaxel-loaded PLGA nanoparticles to increase pharmacological sensitivity in MDA-MB-231 and MCF-7 breast cancer cells

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**ABSTRACT** This study aimed to develop docetaxel (DTX) loaded poly(lactic-co-glycolic acid) (PLGA) nanoparticles (DTX-NPs) and to evaluate the different pharmacological sensitivity of NPs to MCF-7 and MDA-MB-231 breast cancer cells. NPs containing DTX or coumarin-6 were prepared by the nanoprecipitation method using PLGA as a polymer and d- $\alpha$ -tocopherol polyethylene glycol 1000 succinate (TPGS) as a surfactant. The physicochemical properties of NPs were characterized. *In vitro* anticancer effect and cellular uptake were evaluated in breast cancer cells. The particle size and zeta potential of the DTX-NPs were  $160.5 \pm 3.0$  nm and  $-26.7 \pm 0.46$  mV, respectively. The encapsulation efficiency and drug loading were  $81.3 \pm 1.85\%$  and  $10.6 \pm 0.24\%$ , respectively. The *in vitro* release of DTX from the DTX-NPs was sustained at pH 7.4 containing 0.5% Tween 80. The viability of MDA-MB-231 and MCF-7 cells with DTX-NPs was  $37.5 \pm 0.5\%$  and  $30.3 \pm 1.13\%$ , respectively. The  $IC_{50}$  values of DTX-NPs were 3.92- and 6.75-fold lower than that of DTX for MDA-MB-231 cells and MCF-7 cells, respectively. The cellular uptake of coumarin-6-loaded PLGA-NPs in MCF-7 cells was significantly higher than that in MDA-MB-231 cells. The pharmacological sensitivity in breast cancer cells was higher on MCF-7 cells than on MDA-MB-231 cells. In conclusion, we successfully developed DTX-NPs that showed a great potential for the controlled release of DTX. DTX-NPs are an effective formulation for improving anti-cancer effect in breast cancer cells.

## INTRODUCTION

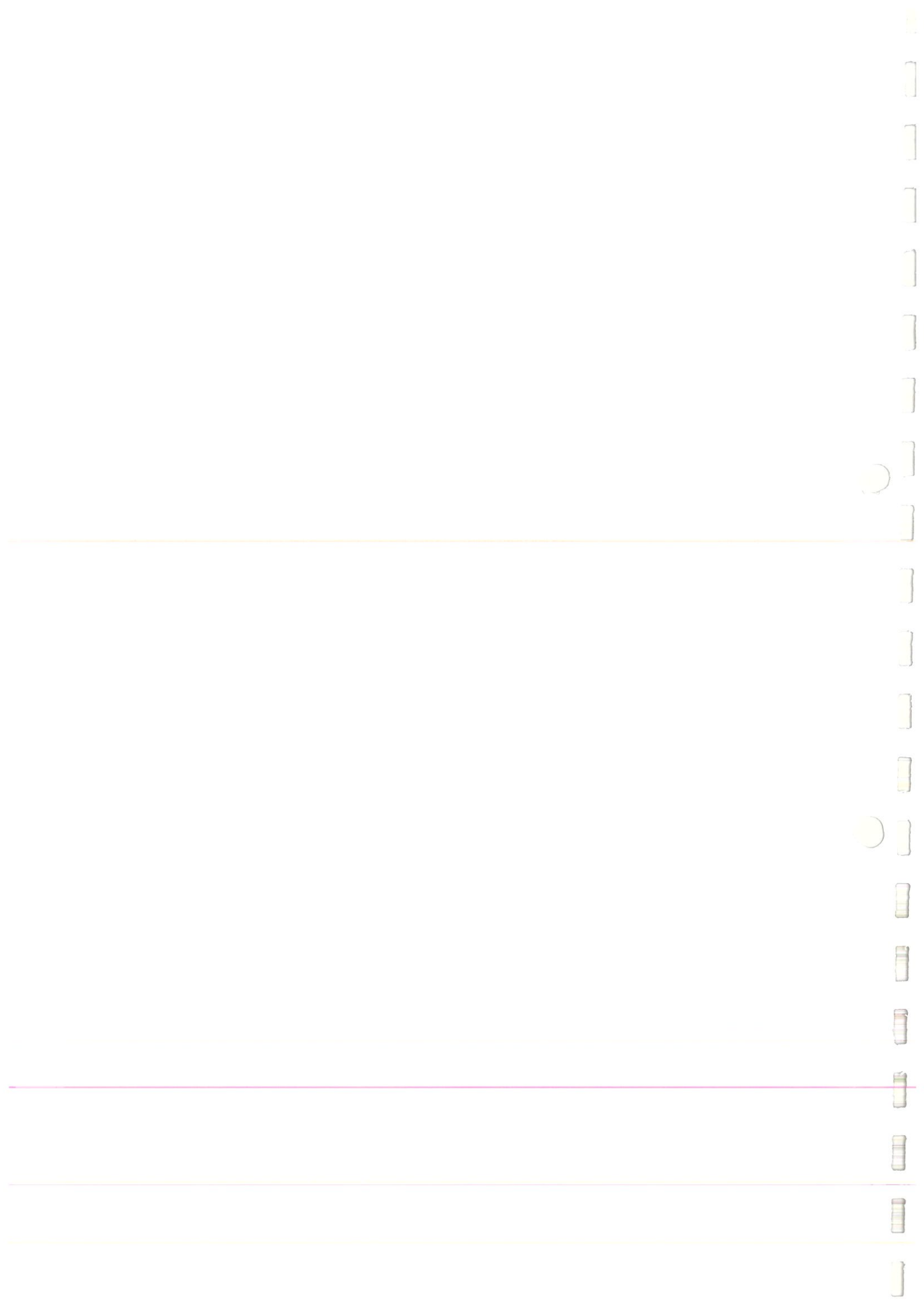
Breast cancer occurs when some breast cells begin to grow abnormally and divide more rapidly than healthy cells. These cells accumulate and form a lump or mass. Breast cancer cells can spread to the lymph nodes and other parts of the body. Therefore, the development of a drug with high efficacy in the treatment of breast cancer would play an important role in reducing the death rate of woman with this disease. Many drugs are currently used to treat breast cancer such as doxorubicin [1], gemcitabine [2], paclitaxel [3], docetaxel (DTX) [4], and leuprolide [5]. Among them, DTX is a second-generation taxane approved by the US

Food and Drug Administration (FDA) to treat multiple types of cancers such as breast, non-small cell lung, hormone-refractory prostate cancers, and gastric adenocarcinoma and squamous cell carcinoma of the head and neck [6]. DTX is usually selected as a model drug for the treatment of breast cancer and it acts as a microtubule-stabilizing agent that blocks the cell cycle at the G2/M phase, which inhibits microtubule disassembly during cell-cycle progression, causing cell death. It is designated as biopharmaceutical classification system class IV agent that has poor aqueous solubility and permeability, which reduce its bioavailability, thereby limiting the treatment efficacy. Therefore, the commercial DTX product Taxotere (Sanofi Aventis, Bridgewater, NJ, USA)



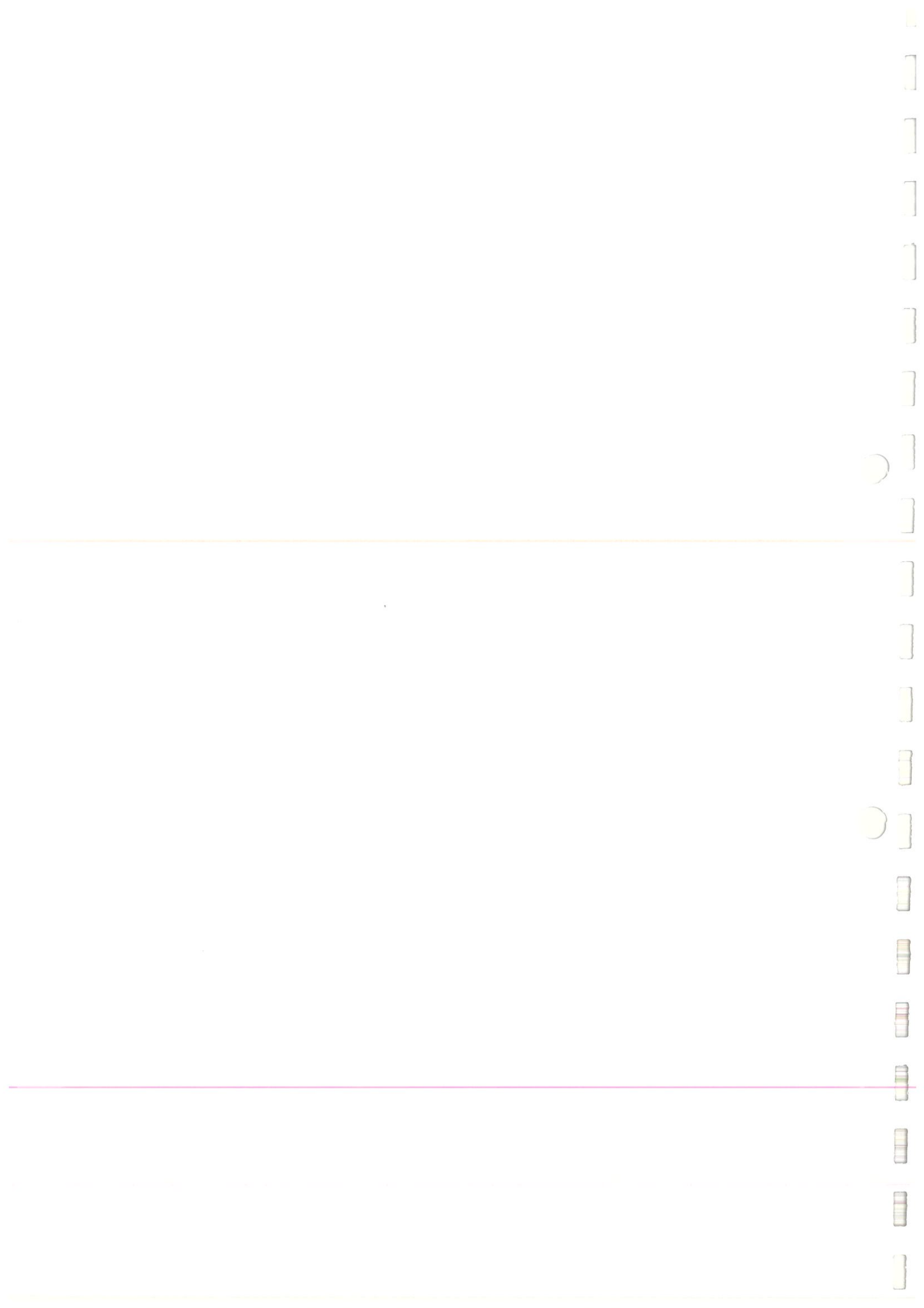
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**Author contributions:** P.T. designed the study and wrote the manuscript. T.N.N. performed the HPLC analysis. Y.L. and P.N.T. performed the cell-based assay experiments. J.S.P. supervised and coordinated the study.

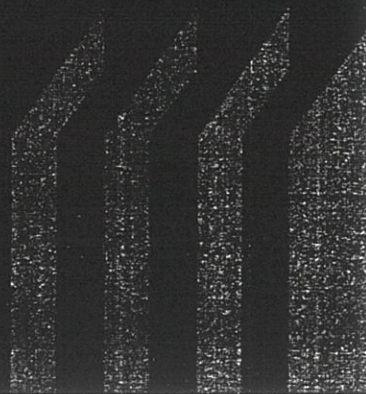


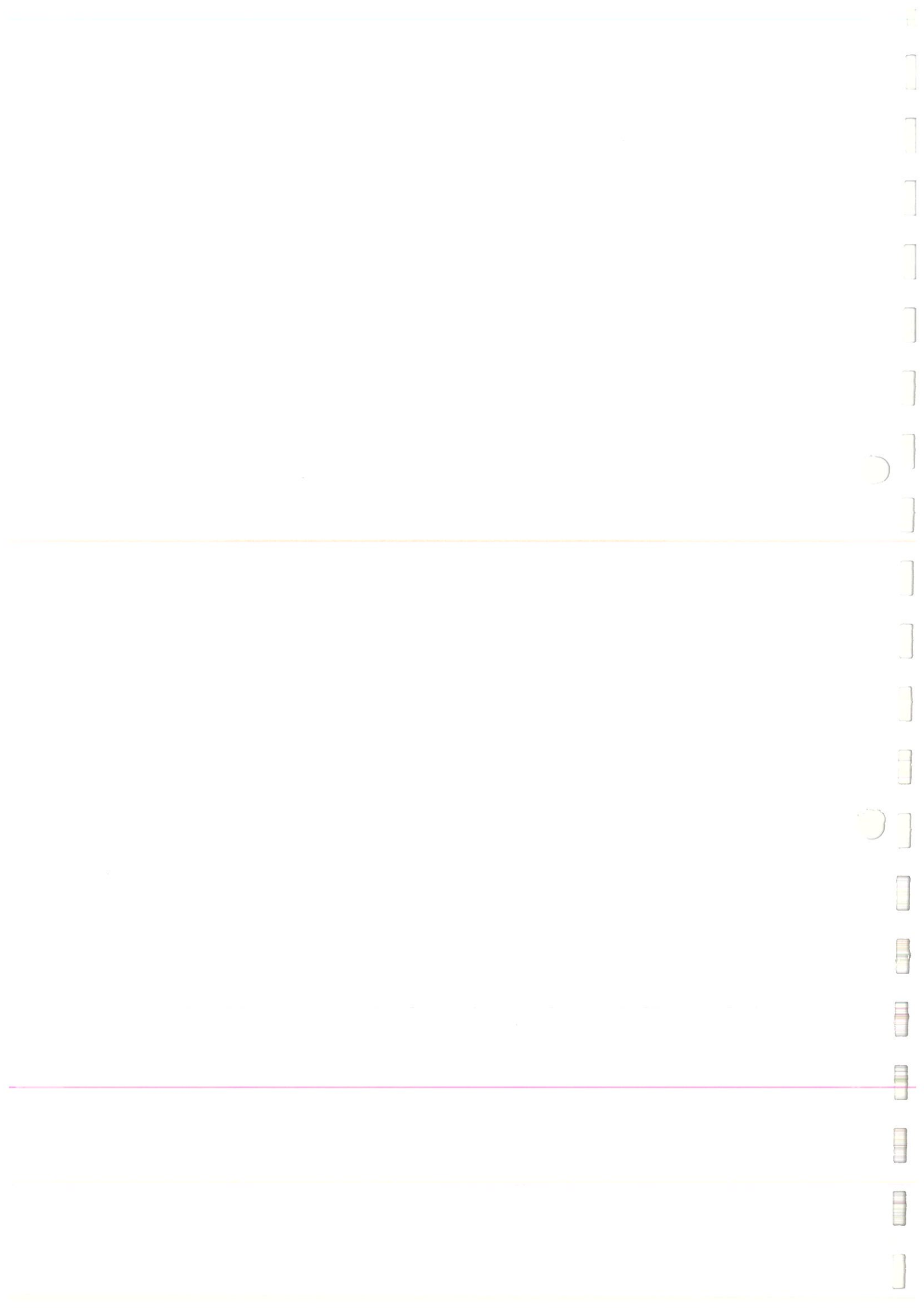


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PHARMACEUTICAL  
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RESEARCH ARTICLE



# Formulation of solid dispersion to improve dissolution and oral bioavailability of poorly soluble dexibuprofen

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## ABSTRACT

Dexibuprofen (DEXI) belongs to BCS class II drug with poor aqueous solubility resulting in poor bioavailability. To enhance solubility and bioavailability of DEXI, DEXI-loaded solid dispersion (SD) was formulated. DEXI-SDs were prepared by melting method and solvent evaporation method. Amphipathic polymer poloxamer 407 (pol 407) was selected based on solubility and dissolution tests. The ratio of DEXI:pol 407 was optimized as 1:2. The physicochemical properties, dissolution, and oral bioavailability of SD3 and SD6 were evaluated to compare preparation methods. The dissolution rate of DEXI from SD formulations was higher at pH 6.8 and pH 7.2 than at pH 1.2. Following oral administration in rats, the  $C_{max}$  and  $AUC_{last}$  of SD3 and SD6 formulations were significantly higher compared with raw DEXI. In addition, the SD6 formulation showed increased  $C_{max}$  and  $AUC_{last}$  by 1.34- and 1.33-fold, compared with those of SD3 formulation, respectively. These results demonstrated that SD formulation has excellent potential as a formulation for poorly soluble drug DEXI.

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## KEYWORDS

Dexibuprofen; solid dispersion; dissolution; bioavailability

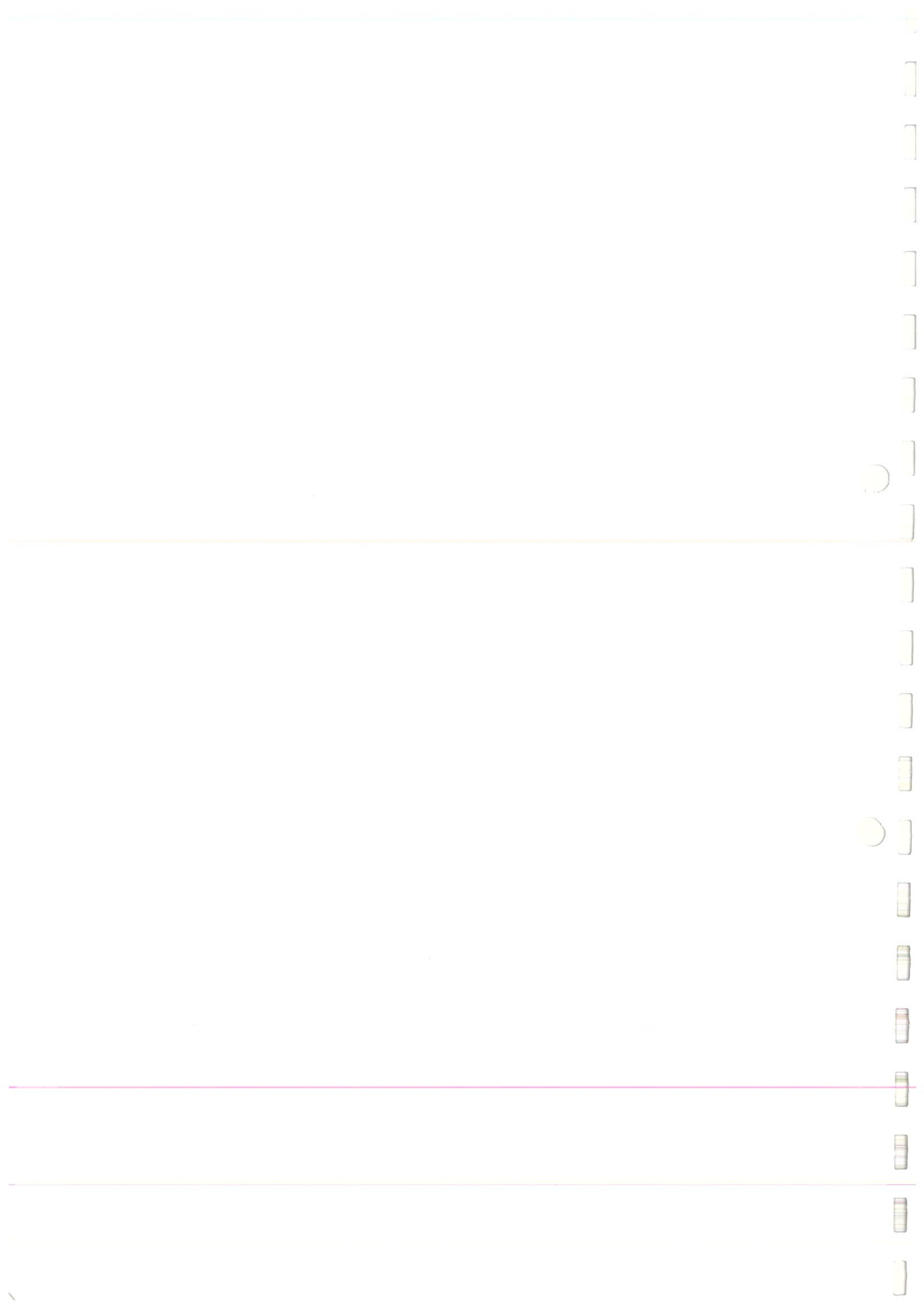
## 1. Introduction

Currently, oral administration is the preferred route of treatment, owing to several advantages such as convenience, avoidance of pain, and safety. The prerequisite for oral administration is complete and predictable absorption in the gastrointestinal (GI) tract. To achieve this, drugs should dissolve in water to be absorbed in the GI tract and be effectively taken up in the circulatory system. However, approximately 40% of new chemical entities (NCEs) are reportedly as poor water-soluble drugs (hydrophobic drugs) resulting in incomplete absorption, poor bioavailability (BA), and large inter- and intra-individual variability in drug concentrations *in vivo*. Thus, enhancing the dissolution and BA of poorly water-soluble drugs are great challenges in the pharmaceutical industry (Singh et al. 2018).

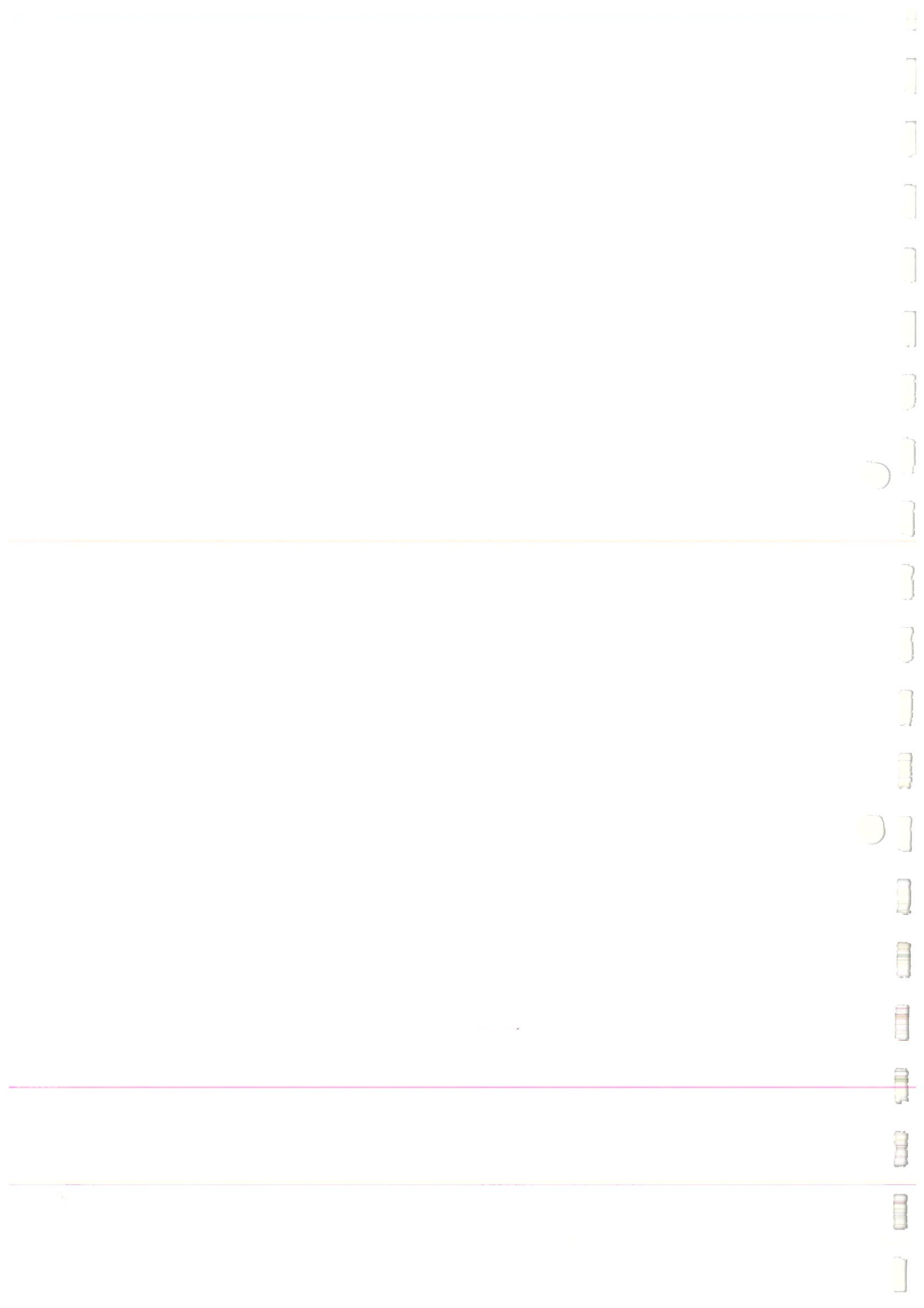
Dexibuprofen (DEXI) (*S*-(4-isobutyl phenyl)-propionic acid), a nonsteroidal anti-inflammatory drug, is typically used in the treatment of osteoarthritis, acute and chronic pain, rheumatoid arthritis, and related conditions (Bondan et al. 2017; Gordo et al. 2017; Ho et al. 2018). DEXI is an *S*+ enantiomer of ibuprofen and belongs to Biopharmaceutics Classification System class II with low solubility (around 11  $\mu\text{g}/\text{mL}$ ) and high permeability (Kaehler et al. 2003; Rinaki et al. 2004; Potthast et al. 2005; Tsume et al. 2012; Stoyanova et al. 2016). The high permeability of ibuprofen and its enantiomers have been observed in Caco-2 cell cultures. In a radiolabeled Caco-2 cell culture study, the apparent permeability coefficient ( $P_{app}$ ) of ibuprofen was  $30.1 \times 10^{-6} \text{ cm/s}$  (Berben et al. 2018). Due to its low solubility, the dissolution rate of DEXI is limited in the GI tract, thereby decreasing the BA of the drug. Thus, improving the solubility and dissolution rate of DEXI can enhance the BA of the drug. Therefore, several techniques have been developed to improve the drug solubility and BA (Karashima et al. 2017; Ahsan and Verma 2018; Choi et al. 2019a).

Solid dispersion (SD) is well-studied technique used to enhance solubility and BA of poorly water-soluble drugs (Mehenni et al. 2018; Ding et al. 2019; Kwon et al. 2019). SD is defined as a group of solid products consisting of a hydrophobic drug dispersed in at least one hydrophilic carrier, resulting in an enhanced surface area, and leading to higher drug solubility and dissolution rate. Enhanced drug BA is achieved by improving wettability and dispersibility, and reducing the aggregation and agglomeration of drug particles (Tran et al. 2019). Besides the traditional methods to produce SD as melting method, solvent evaporation method, spray-dried amorphous SD has recently used (Henriques et al. 2021). The selection of suitable carrier is a prerequisite for success in formulation. Soliman et al. prepared diacerein solid dispersion loaded tablets to enhance solubility, dissolution, and BA of diacerein using Pluronic® F68 (poloxamer 188) as the carrier (Soliman et al. 2021). As the result, the solubility of diacerein from SD (187.61  $\mu\text{g}/\text{mL}$ ) was 8.3-fold higher compared to drug powder (22.5  $\mu\text{g}/\text{mL}$ ). While the dissolution rate of SD was 6.6-fold higher than powder drug, the dissolution rate of SD tablet was 12.5-fold higher than the marketed product. In addition, the oral BA of diacerein from SD tablet was improved 2.66-fold in comparison with the marketed product.

In this study, DEXI-SD formulations were prepared by melting method and solvent evaporation method. (2-hydroxypropyl)- $\beta$ -cyclodextrin (HP- $\beta$ -CD), hydroxypropyl cellulose (HPC), polyvinylpyrrolidone (PVP), urea, poloxamer 188 (pol188), poloxamer 407 (pol407), and PEG 6000 were screened to select the suitable carrier. The physicochemical properties of SD formulations were evaluated using a field emission scanning electron microscope (FE-SEM), powder X-ray diffraction (PXRD), differential scanning calorimetry (DSC), and Fourier-transform infrared spectroscopy (FTIR). *In vitro* dissolution, *in vitro* cytotoxicity, and a pharmacokinetic study of DEXI were also evaluated.



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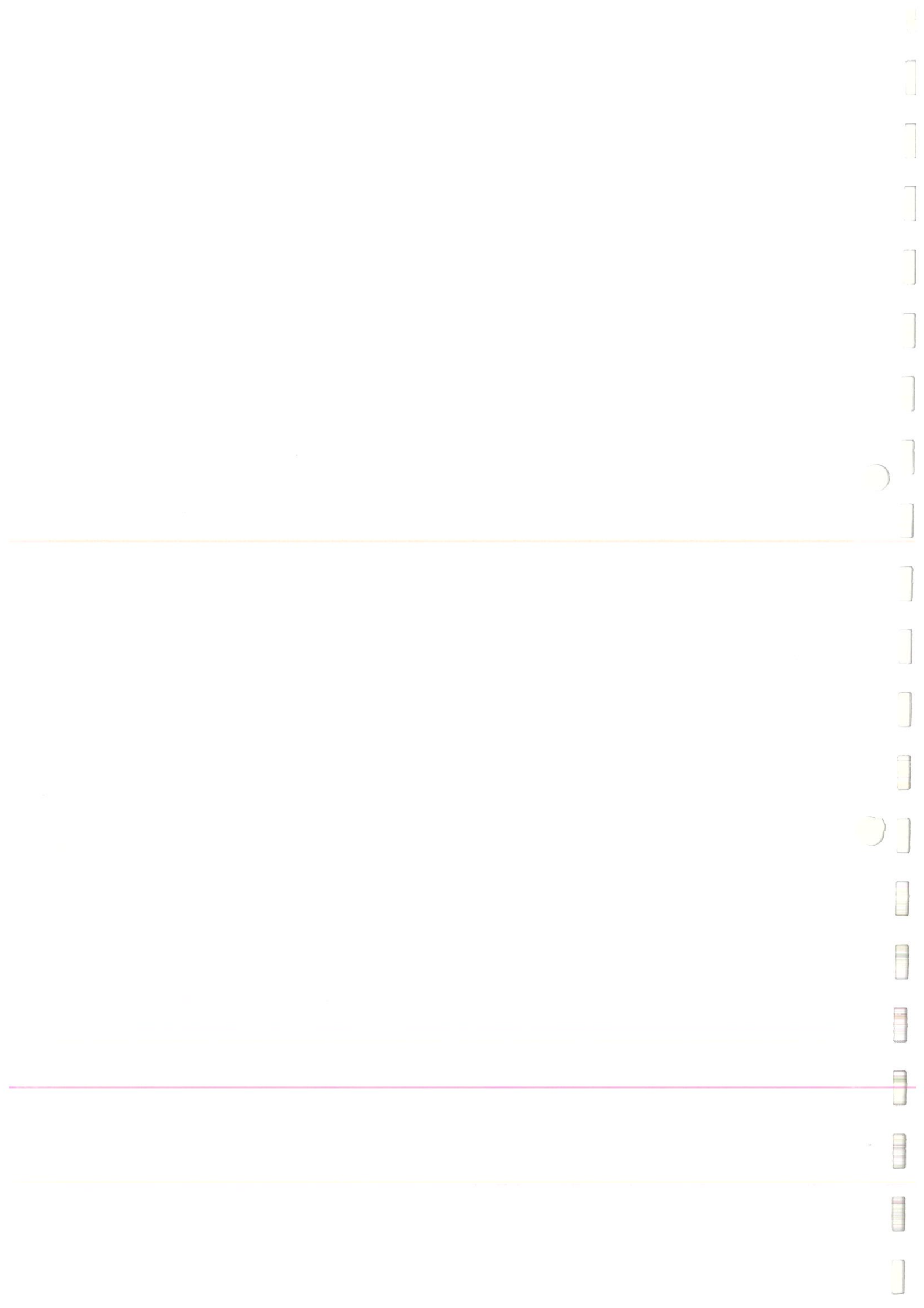
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REVIEW



# Recent trends of self-emulsifying drug delivery system for enhancing the oral bioavailability of poorly water-soluble drugs

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## Abstract

**Background** The oral route is the most popular route for the clinical administration of drugs to treat various diseases. Before a drug is absorbed into the blood circulation, it must undergo dissolution and permeation. However, most drugs exhibit poor aqueous solubility, and their limited absorption leads to low oral bioavailability. The solubility of hydrophobic drugs can be improved by various ways, such as solid dispersion, salt formation, pH modification, and self-emulsifying drug delivery system (SEDDS) use. Among them, the SEDDS has garnered attention during recent years as it improves oral bioavailability, reduces drug dose, and increases drug protection from unsuitable environment in the gastrointestinal tract.

**Area covered** SEDDS comprises lipid-based formulations. It can solve the problems related to the dissolution and bioavailability of the Biopharmaceutics Classification System Class II and IV drugs. Depending on the preparation procedure, drug-loaded SEDDS can be divided into micro- (SMEDDS) and nano- (SNEDDS) formulations. In this review, we summarize the classification system of lipid formulations, the mechanism underlying improved oral drug absorption by SEDDS, and recent advances in the SEDDS.

**Expert opinion** The SEDDS is a potential formulation for drug delivery. Owing to its small particle size, large surface area, high encapsulation efficiency, and high drug loading, the SEDDS can improve the rate and extent of oral absorption by maximizing drug solubility in the intestinal absorption site. Moreover, because of the lipid-based formulation of SEDDS, it can stimulate and enhance lymphatic transport of drugs to avoid hepatic first-pass metabolism, and thus improve their bioavailability.

**Keywords** SEDDS · Oil · Surfactant · Co-surfactant/co-solvent · Bioavailability

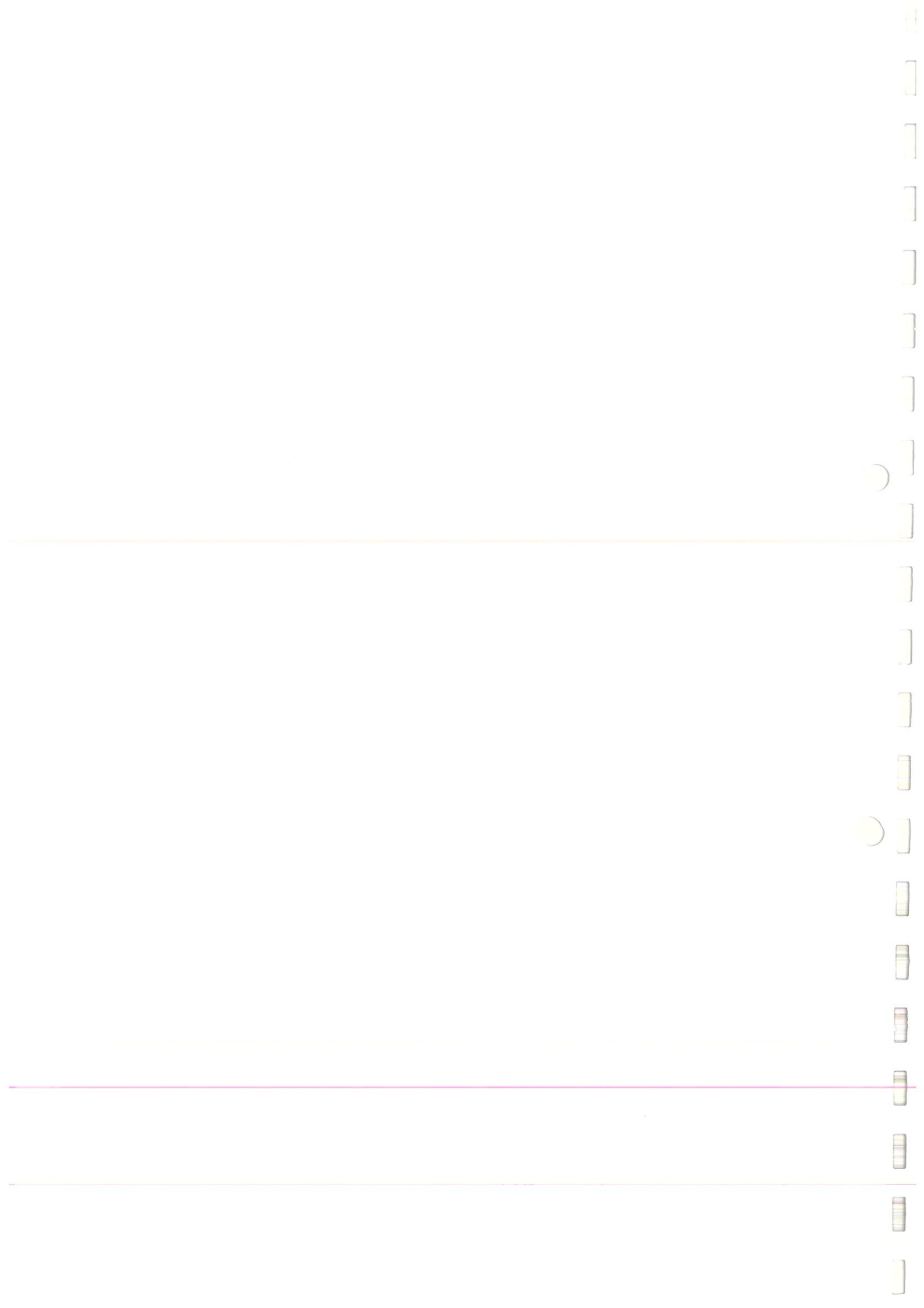
## Introduction

Oral and intravenous (IV) routes are the two most commonly used routes for drug administration. Practically, IV injection is the best administration route for most drugs because 100% of the drug is directly introduced into the blood circulation system. However, IV injections have several limitations including the discomfort from hospitalization, need for sterile needles, difficulty in needle insertion, and need for trained medical staff for IV injection. Therefore, oral administration is currently considered as an attractive route and thus has garnered attention.

Oral administration is safe, easy, and painless. Compared with IV injection, oral administration can be conveniently employed at home by patients without any discomfort. With oral administration, the drug concentration in the blood can be maintained for longer than that with IV injection. Moreover, drugs can be administered orally as liquids, capsules, or solid or chewable tablets. For oral administration, drugs must dissolve in the gastrointestinal (GI) fluid before absorption into the blood circulation (Tran et al. 2019). However, more than 40% of new chemical entities (NCEs) are insoluble in water (Takagi et al. 2006; Kawabata et al. 2011; Rodriguez-Aller et al. 2015), resulting in poor absorption and low bioavailability (BA). In general, drug absorption is mainly influenced by two factors, namely, solubility and permeability. Amidon et al. first introduced the Biopharmaceutics Classification System (BCS) based on these two factors (Amidon et al. 1995). Drugs are divided into four groups as shown in Fig. 1 (FDA 2017; Nikolakakis and Partheniadis

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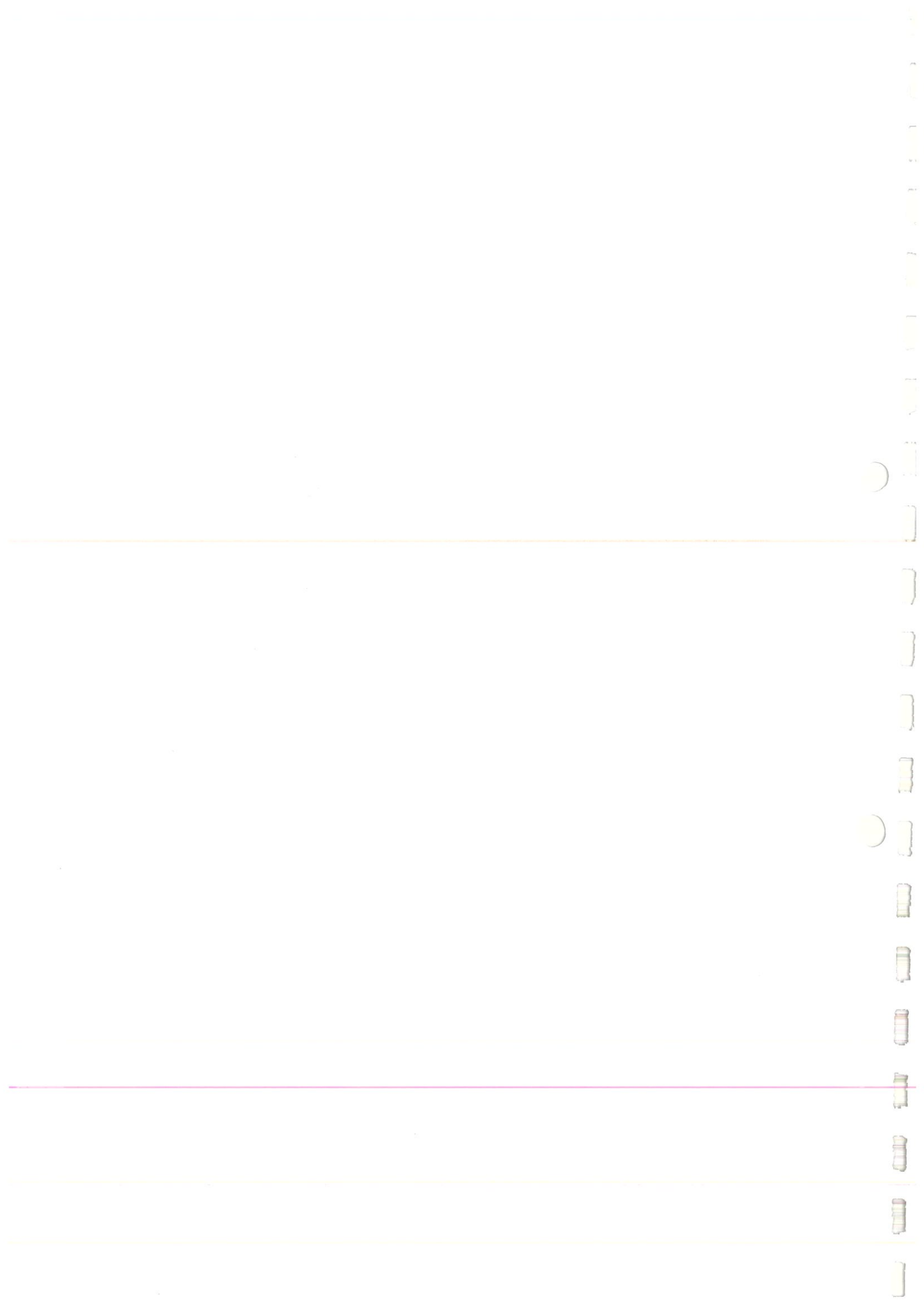
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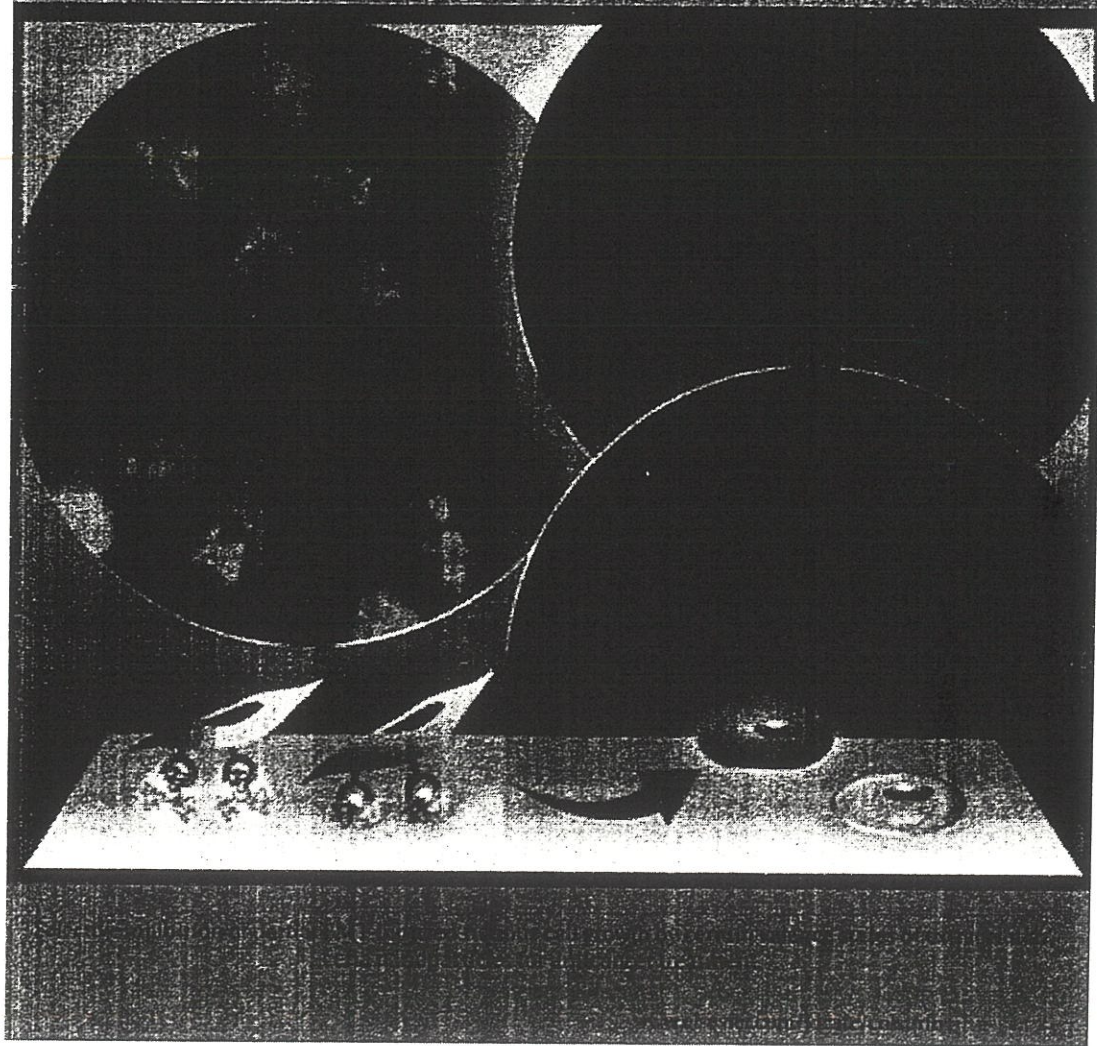
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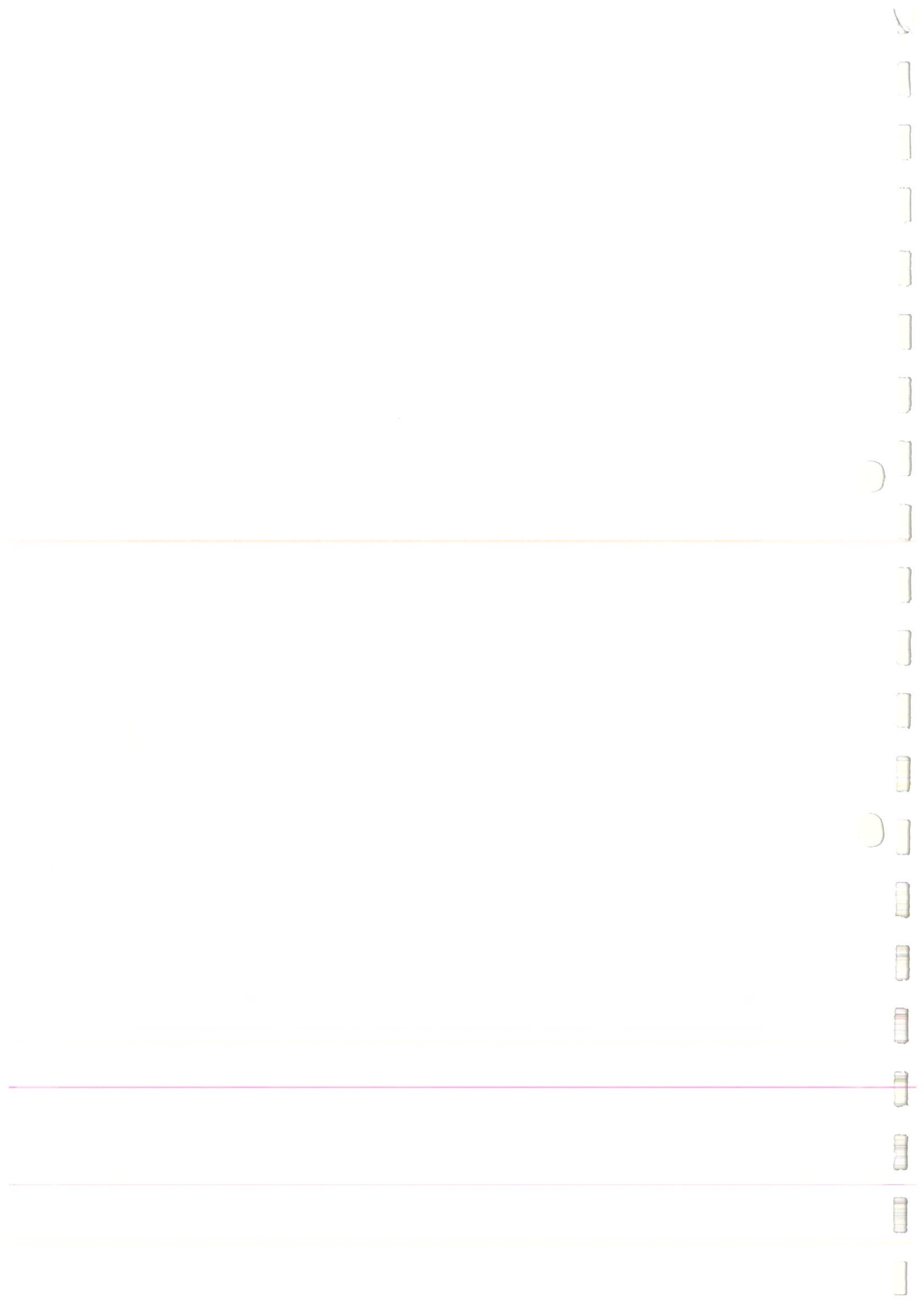
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# COLLOIDS AND SURFACES B

Biointerfaces











# Chitosan-coated nanostructured lipid carriers of fenofibrate with enhanced oral bioavailability and efficacy

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## ARTICLE INFO

**Keywords:**  
fenofibrate  
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carrier  
poorly soluble

## ABSTRACT

Fenofibrate is frequently used to lower cholesterol levels in cardiovascular disease. Owing to its poor solubility and high gastrointestinal permeability, it is classified as a Biopharmaceutics Classification System class II compound. The aim of this study was to improve the solubility and bioavailability of fenofibrate by formulating it as fenofibrate-loaded nanostructured lipid carriers (FFB-NLCs) and coating it with a biodegradable polymer to allow controlled drug release. Chitosan-coated nanostructured lipid carriers (CF-NLCs) were prepared via an ultrasonication method using chitosan as the biodegradable polymer, stearic acid as the solid lipid, oleic acid as the liquid lipid, and Tween 80 as the surfactant. To study encapsulation efficiency and solubility conditions, stearic acid/oleic acid ratios were varied as 80/20, 70/30, 60/40, and 50/50 (mg/mg), by adjusting chitosan ratio. Chitosan is an adhesive polymer, coating the surface of the NLC to improve its bioavailability. All NLC formulations demonstrated a particle size of approximately 200 nm and a polydispersity index below 0.3. The encapsulation efficiencies of the NLC formulations were above 85%. For CF-NLCs, the solubility and encapsulation efficiency of fenofibrate were increased when compared with those of a commercial fenofibrate formulation. The pharmacokinetic and pharmacodynamic parameters of fenofibrate in the form of CF-NLCs were improved after oral administration. CF-NLCs can be used for allowing controlled release and improving the bioavailability and stability of fenofibrate.

## 1. Introduction

Recently discovered novel drug candidates are insoluble in the aqueous phase [1]. Despite their excellent efficacy, some candidates are limited in therapeutic use owing to their poor aqueous solubility [2]. Novel concepts are crucial to address this shortcoming. One strategy is to develop a carrier that can be encapsulated, protected, and released under specific and desired conditions [3]. As guest molecules electrostatically enter the hydrophobic matrix, lipid materials are suitable candidates for the formulation of active hydrophobic delivery systems. Furthermore, various techniques, additives, and formulations are required to enhance the solubility of poorly soluble drugs. Self-emulsifying drug delivery systems (SEDDS) [4], self-microemulsifying drug delivery systems (SMEDDS) [5–7], amorphous solid dispersions [8], nanosuspensions [9], and liquid crystals [10,11] have been tested. Several lipid-based carriers have been established including emulsions, liposomes, solid lipid nanoparticles (SLNs), as well as the more recently developed, nanostructured lipid carriers (NLCs).

Fenofibrate, a biopharmaceutical classification system class II drug, is used to treat hypercholesterolemia and hypertriglyceridemia [8]. Fenofibrate is marketed globally and has been well-described pharmacologically [12]. The drug is poorly water-soluble, partly owing to its high hydrophobicity ( $\log P = 5.24$ , Fig. S1). Therefore, it exhibits poor oral bioavailability. For poorly water-soluble drugs, the rate of absorption depends on the rate of dissolution, which in turn determines the bioavailability [13]. Lipidil® Supra, a brand name for fenofibrate, has been used commercially for the treatment of hyperlipidemia (Green Cross Co., Ltd., Seoul, Korea), and is consumed orally once a day.

It is challenging to administer lipid-based drug carriers as enzymatic hydrolysis by lipase causes rapid elimination of particles, resulting in the loss of a certain amount of bioactive molecules. Hence, these particles should be protected from gastrointestinal environment. Polymer coating and encapsulation of nanoparticles in polymeric microparticles (synthetic and natural polymers) have been used to protect the formulation from enzymatic attack. A polymer coating system with natural polymers (e.g., hyaluronic acid and chitosan) improves the oral bioavailability of bioactive molecules [14]. This strategy was applied to develop NLCs

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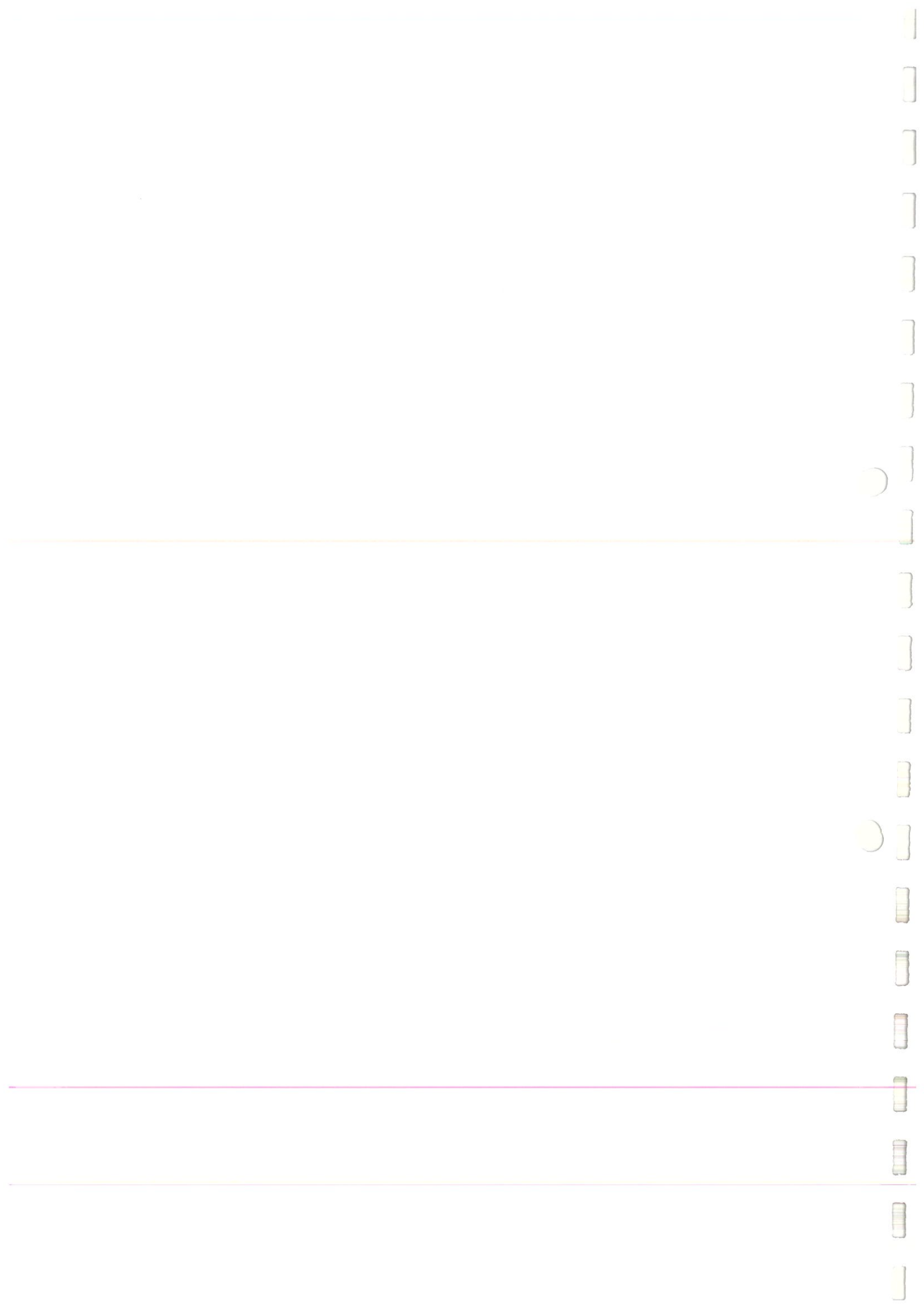
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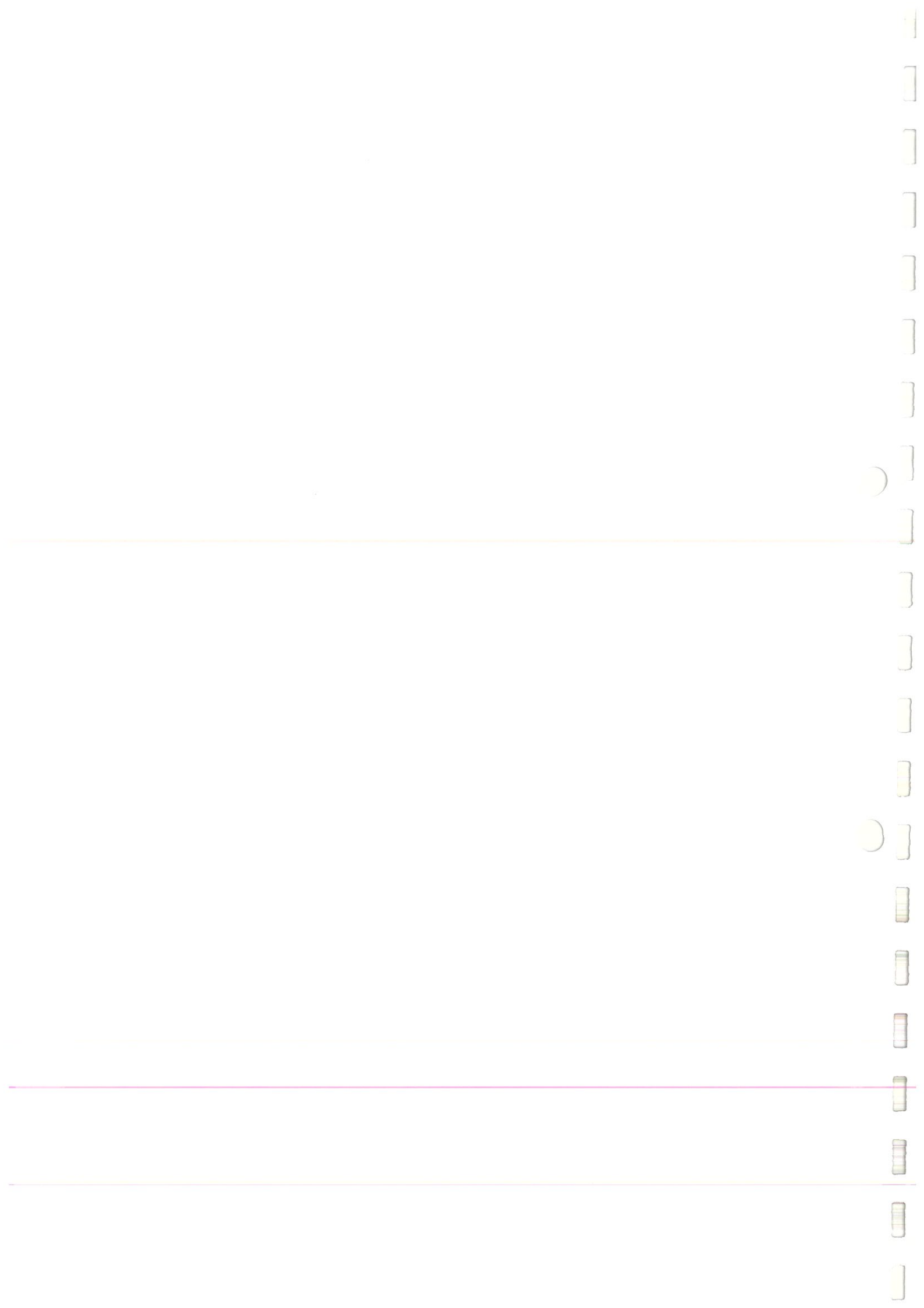
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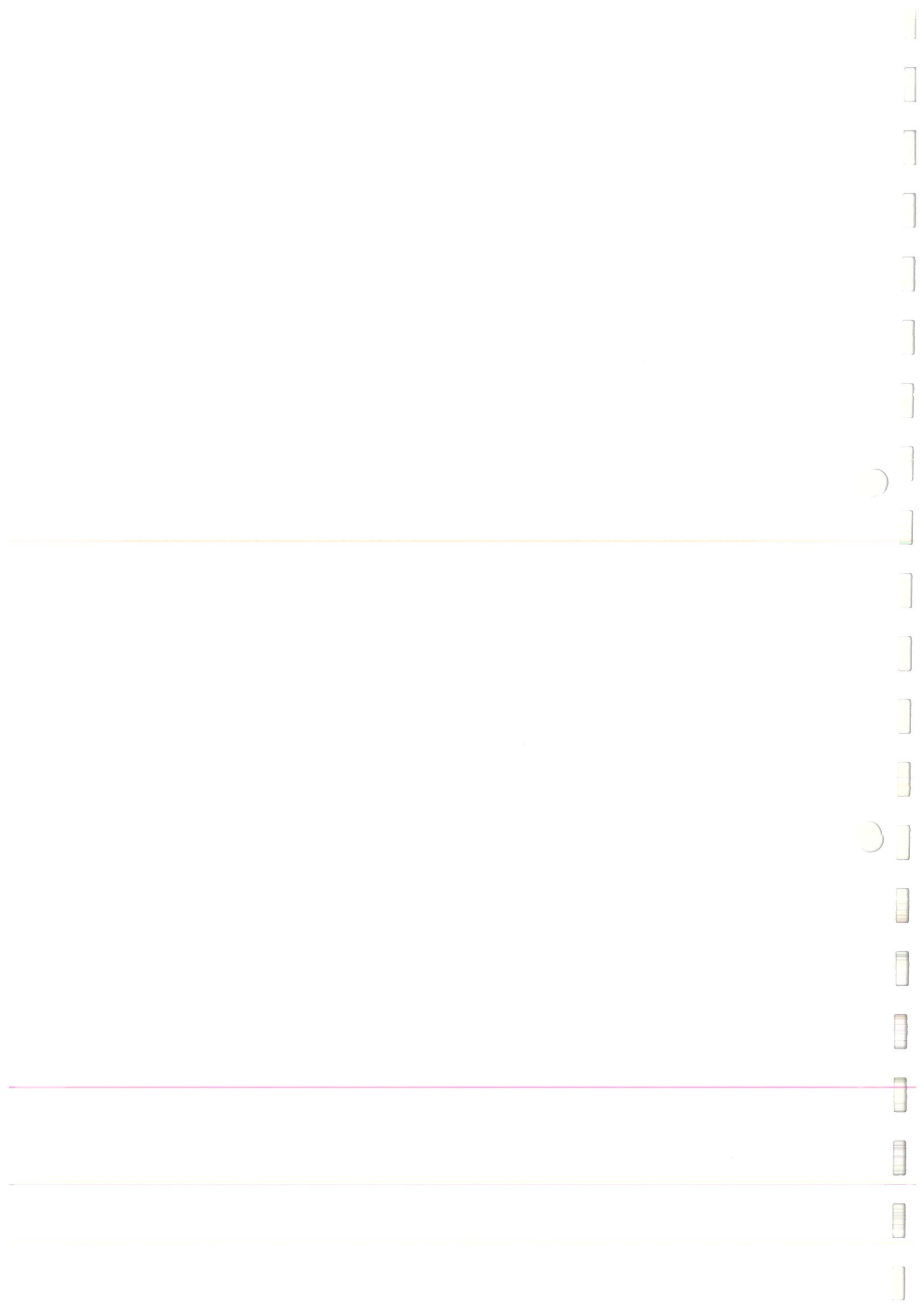
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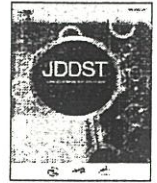
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## Effect of calcium chloride on the protein encapsulation and stability of proliposomal granules

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Cytotoxicity

### ABSTRACT

The purpose of this study was to develop oral proliposomal granules incorporating CaCl<sub>2</sub> in order to enhance the encapsulation efficiency (EE) of protein model drug after reconstitution. Proliposomal granules were prepared by a granulation process with a solid carrier, protein model drug, and lipid solution. The proliposomal granules were characterized in terms of particle size, EE, and loading capacity. Protein structure analysis and cellular viability were also examined. CaCl<sub>2</sub>, ranged 0.125–6.0% w/w, was successfully incorporated into the dried granules during the wet binding process of granulation. Reconstituted proliposomes with 1% w/w CaCl<sub>2</sub> showed the highest EE among those examined. Different reconstituted diluents did not alter the EE, but had an impact on particle size and charge. The  $\alpha$ -helical content (%), calculated from the mean molar ellipticity, was similar between protein drug alone and that with addition of CaCl<sub>2</sub>, indicating the preservation of structural integrity, as also confirmed by electrophoresis. CaCl<sub>2</sub>-incorporated proliposomes were non-toxic to cells at the dose used. In conclusion, inclusion of CaCl<sub>2</sub> into proliposomal granules enhanced the EE of protein drug showing optimal effects at 1% w/w with good preservation of protein integrity and cellular viability.

### 1. Introduction

Biotherapeutic agents (biodrugs), such as peptides and proteins, have attracted considerable interest as many of these agents are effective with few side effects [1,2]. However, their lack of stability is still considered as a major concern, especially for the oral administration route [3]. Proliposomes provide advantages for oral administration due to their stability in dried free-flowing powder form, and suitability for formulation as stable oral dosage forms, such as tablets or capsules [4,5]. Tantisripreecha and coworker [6] prepared protein proliposomes by granulation and optimized the preparation conditions. The liposomes reconstituted from proliposomes prepared by this method showed good physical properties, and were well-suited to compressing into tablets. However, the encapsulation efficiency (EE) of reconstituted liposomes was relatively low (10–14%). Other groups also obtained good results with liposomes reconstituted from proliposomes. The EE of salmon calcitonin (sCT) in the reconstituted liposomes was 54.9% and 19.9% for the taurodeoxycholate (TDC) proliposomes and sCT proliposomes, respectively, increasing oral bioavailability of sCT from the TDC proliposomes [7]. The EE of protamine sulfate-recombinant

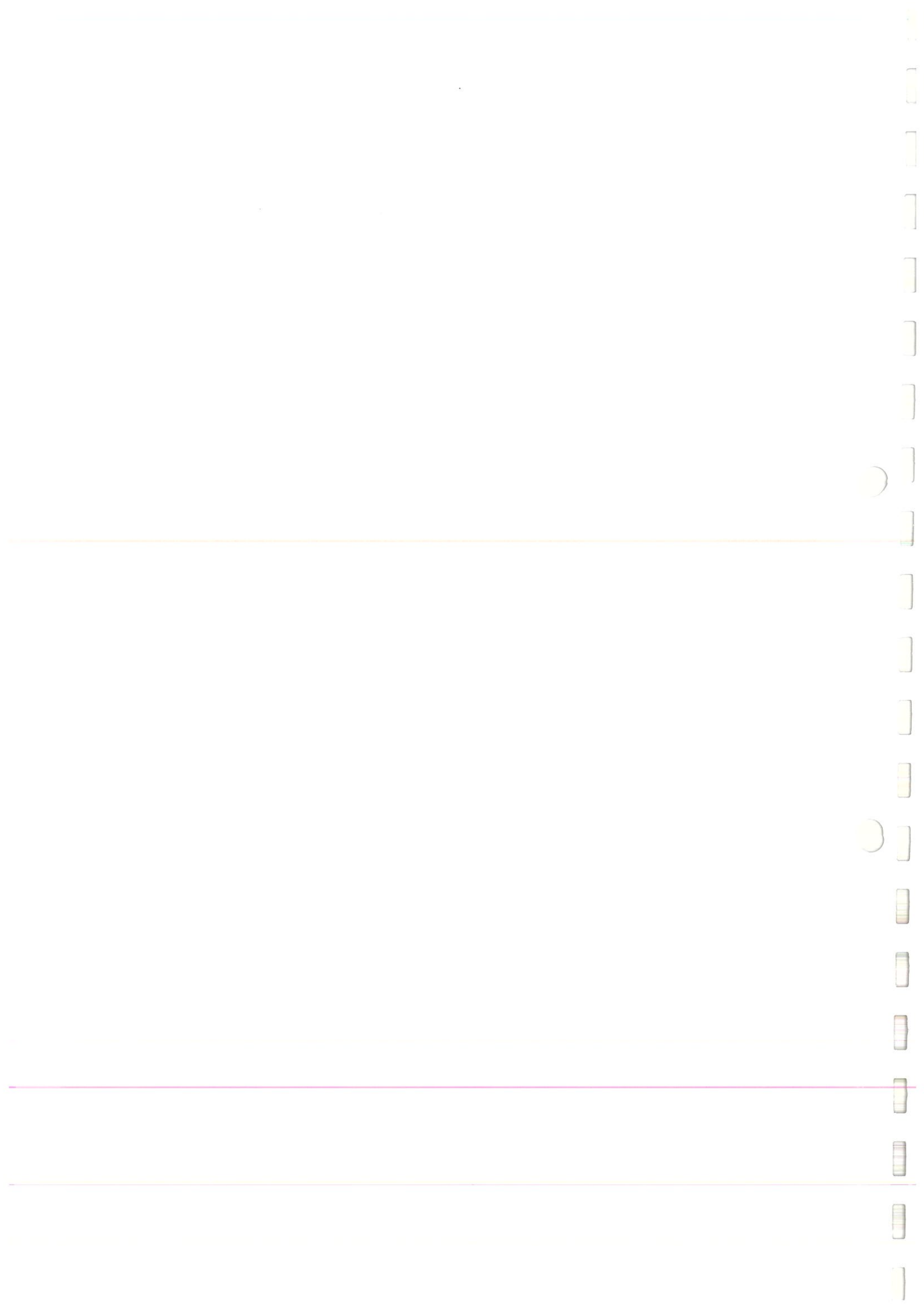
human (Pt-rh) insulin proliposomes was measured to be  $17.6 \pm 2.4\%$  with no significant difference from  $18.7 \pm 4.1\%$  of rh insulin proliposomes, but cellular uptake of Pt-rh insulin proliposomes in Caco-2 cells was superior to that of rh insulin proliposomes [8]. The mannosylated busserelin acetate (MANS-BA) reconstituted from proliposome powders exhibited the 21.12–33.80% of EE, and the permeability of reconstituted MANS-BA liposomes [9]. However, they did not show high EE of peptide/protein drugs [7–9].

Divalent cationic salts have been studied extensively with regard to their effects on binding with biological membranes, i.e., phospholipid bilayers, in biological systems. Interactions occur between cationic salts and the charged phospholipid membrane generally via Coulombic forces [10], with different cationic salts affecting lipid bilayer differently, with respect for example to dissimilar ability to induce membrane aggregation or alter the surface potential of the lipid [11,12]. One common effect of divalent cationic salts is the ability to stabilize the gel state in the gel-to-liquid crystalline phase transition of the phospholipid bilayer. Divalent cationic salts, both calcium and magnesium ions strongly influence the immobilization of phosphodiester groups of phospholipids [10]. These two ions, especially calcium, have

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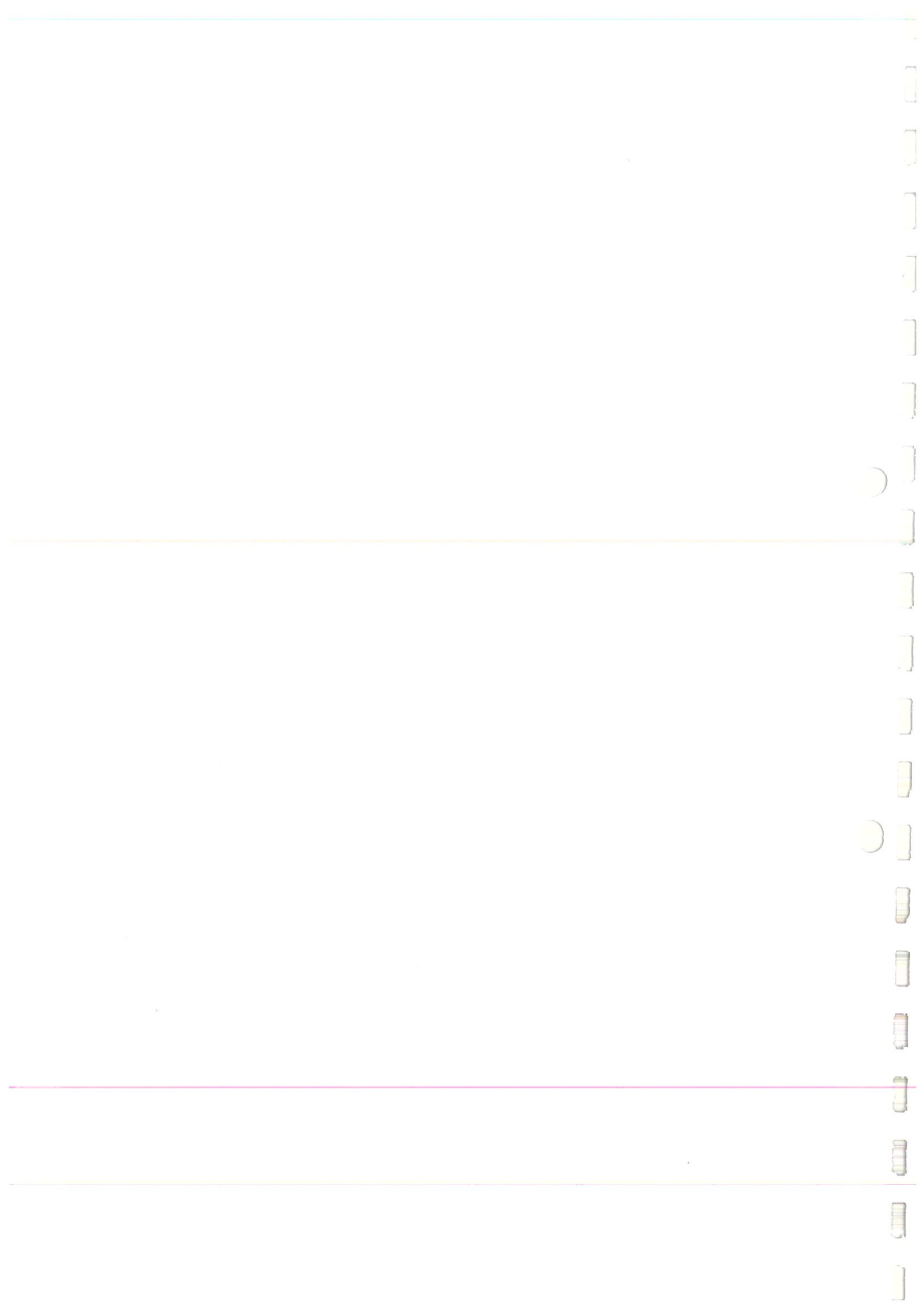
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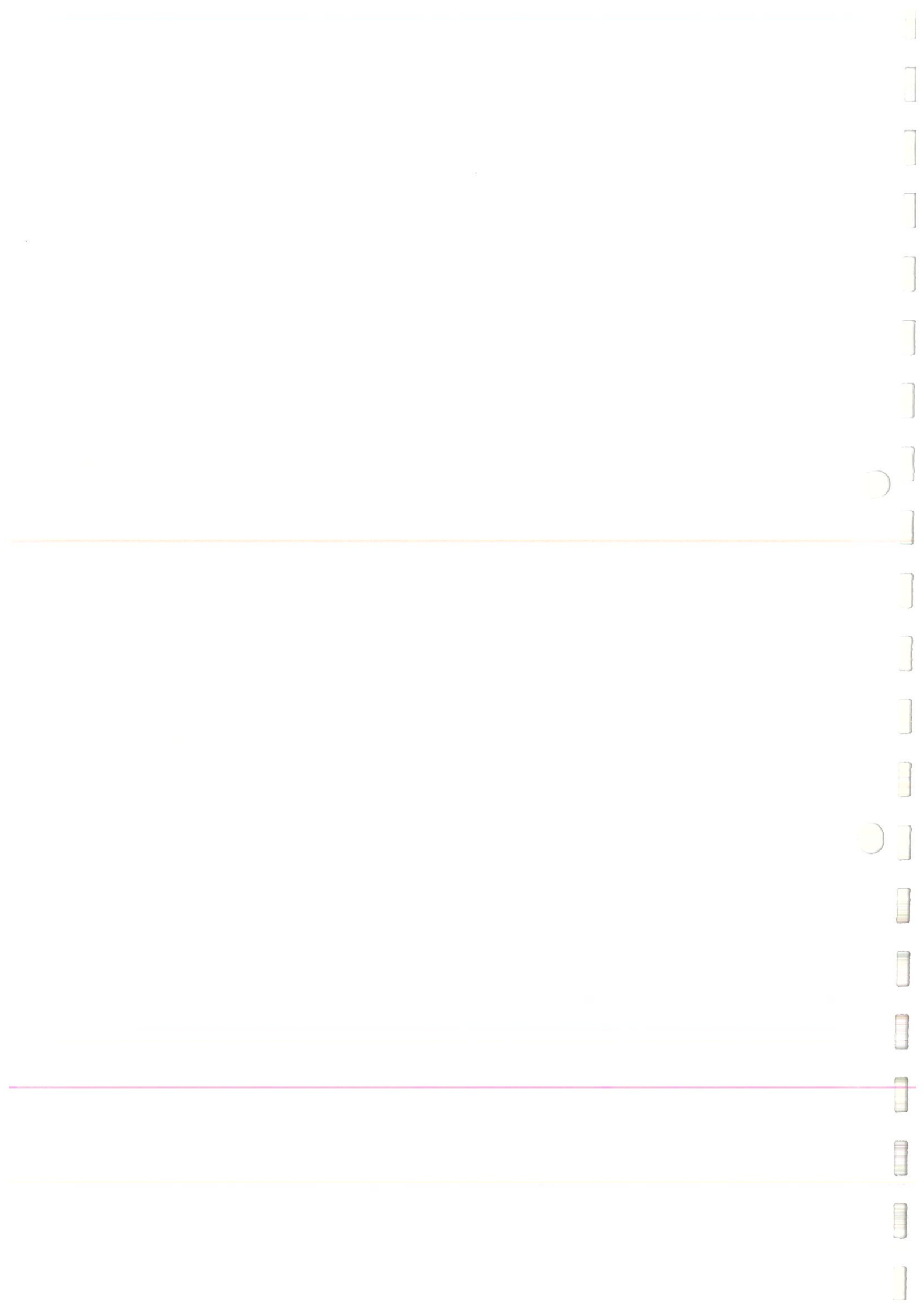
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# Recent advances of nanotechnology for the delivery of anticancer drugs for breast cancer treatment

Phuong Tran<sup>1</sup> · Sang-Eun Lee<sup>1</sup> · Dong-Hyun Kim<sup>1</sup> · Yong-Chul Pyo<sup>1</sup> · Jeong-Sook Park<sup>1</sup>

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## Abstract

**Background** Breast cancer is one of the most common causes of death for women worldwide. While chemotherapy is the treatment option for most cancers, surgery, chemotherapy, and radiotherapy are the three main therapeutic strategies for the treatment of breast cancer. In recent years, nanotechnology applications for cancer treatments have attracted a lot of attention.

**Area covered** This review focuses on the various nanoparticle types, such as liposomes, micelles, polymeric nanoparticles, solid lipid nanoparticles, and gold nanoparticles, and their applications for the treatment of breast cancer.

**Expert opinion** In recent decades, nanotechnology has developed and been applied to cancer treatments. Currently, nanotechnology plays an important role in the targeted delivery of drugs for cancer treatments, including breast cancer. Nanoparticles can target tumors and control the release of drugs to precise sites, thereby improving the therapeutic efficiency of drugs and decreasing the toxicity to normal tissues or organs. In addition, nanoparticles are also able to activate immune cells against tumors. Therefore, nanoparticles are a promising tool for future cancer research and treatment.

**Keywords** Nanoparticles · Breast cancer · Drug delivery · Anticancer drugs

## Introduction

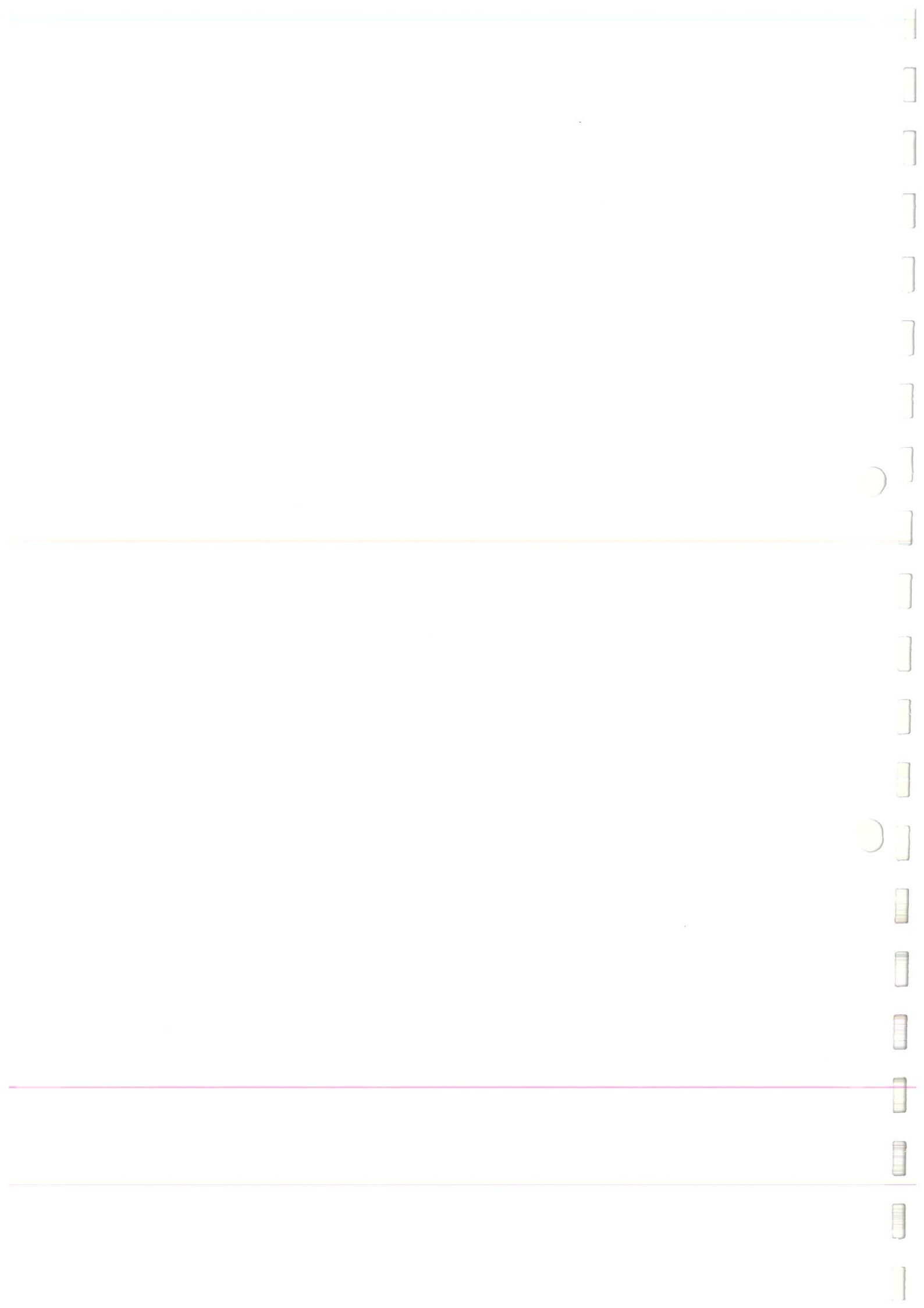
Cancer is one of the leading causes of death worldwide and is defined as a disease that begins when cells grow uncontrollably and crowd out normal cells. Cancer can develop anywhere in the body, such as in the lungs, breasts, or liver. The World Health Organization predicted that the burden of cancer will increase to 23.6 million new cases annually by 2030 (World Health Organization 2014). Thus, cancer treatment has become a prominent issue over the past several decades. For women, breast cancer is one of the most commonly diagnosed cancers globally. In 2018, approximately 266,120 new cases of invasive breast cancer were estimated in women constituting 30% of all cancer cases (878,980 total cases); in addition, 40,920 of these breast cancer cases were estimated to be fatal (American Cancer Society 2018). Breast cancer is usually classified on the basis of the type of receptor overexpression present on the cancer cell membrane (Fig. 1), including progesterone (PR) and estrogen (ER)

hormone receptors and HER2 receptors, with HER2 being a member of the human epidermal growth factor receptor family. Breast cancers that present the overexpression of these receptors are called either PR-, ER-, or HER2-positive, depending on the type of receptor overexpression. Patients that show PR-, ER-, HER2-positive breast cancer cells are said to have triple-positive breast cancer. In addition, triple-negative breast cancer group exists that is composed of breast cancers that are neither PR/ER-positive nor HER2-positive. It has been reported that the primary cause of deaths due to breast cancer is the result of its potential metastasis to distant organs such as the liver, lungs, lymph nodes, bones, and brain (Carty et al. 1995; Grobmyer et al. 2012).

Currently, surgery (in which whole breast is removed, called a mastectomy, or in which only the tumor and surrounding tissues are removed, called a breast-conserving lumpectomy), chemotherapy (in which drugs are used to kill cancer cells), and radiotherapy (in which high-energy waves are used to kill cancer cells) are the three main cancer treatment strategies (Shewach and Kuchta 2009). Among them, chemotherapy is more popularly used for treating most types of cancer. Chemotherapy can kill many cancer cells throughout the body, eradicate microscopic disease at the

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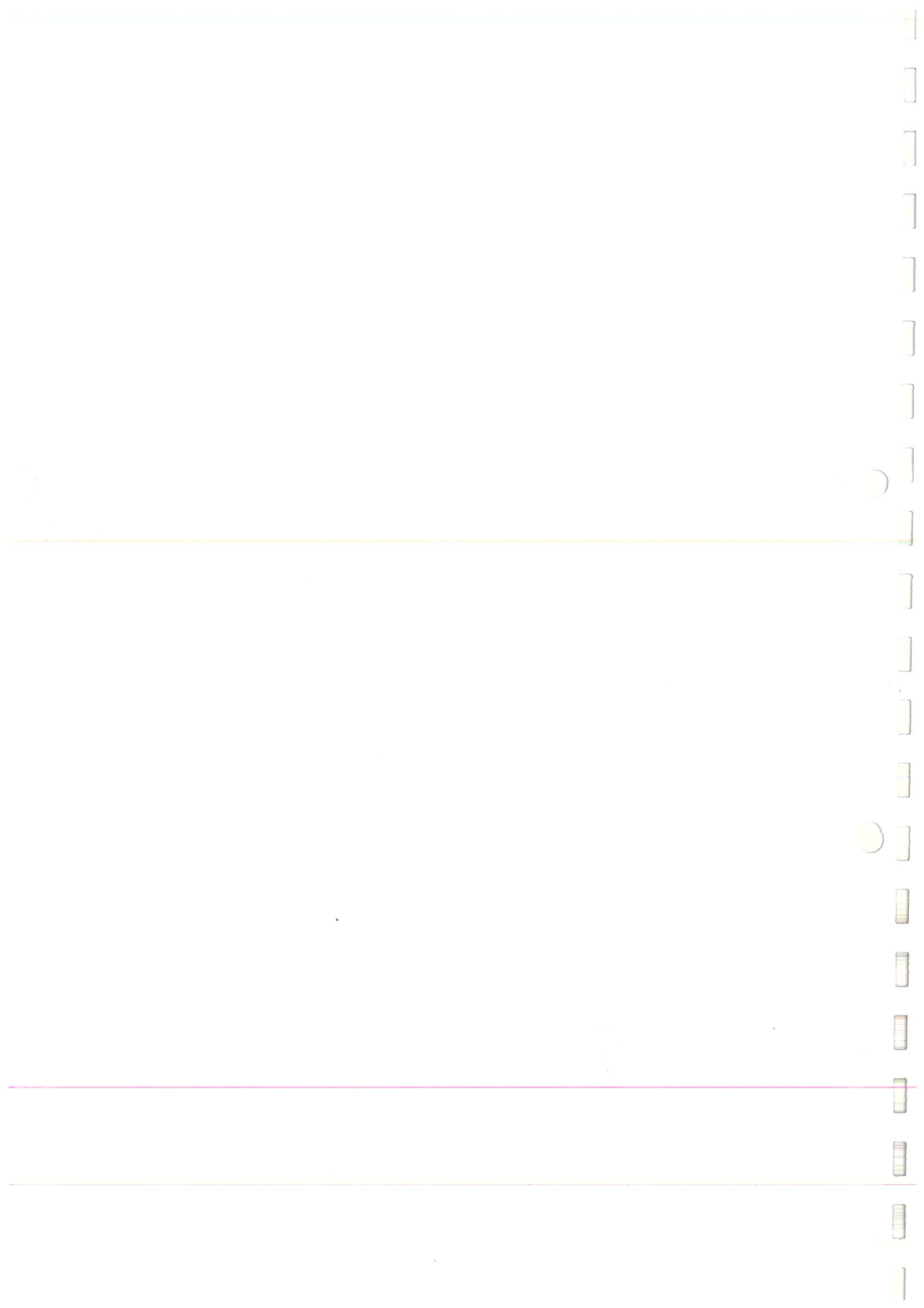
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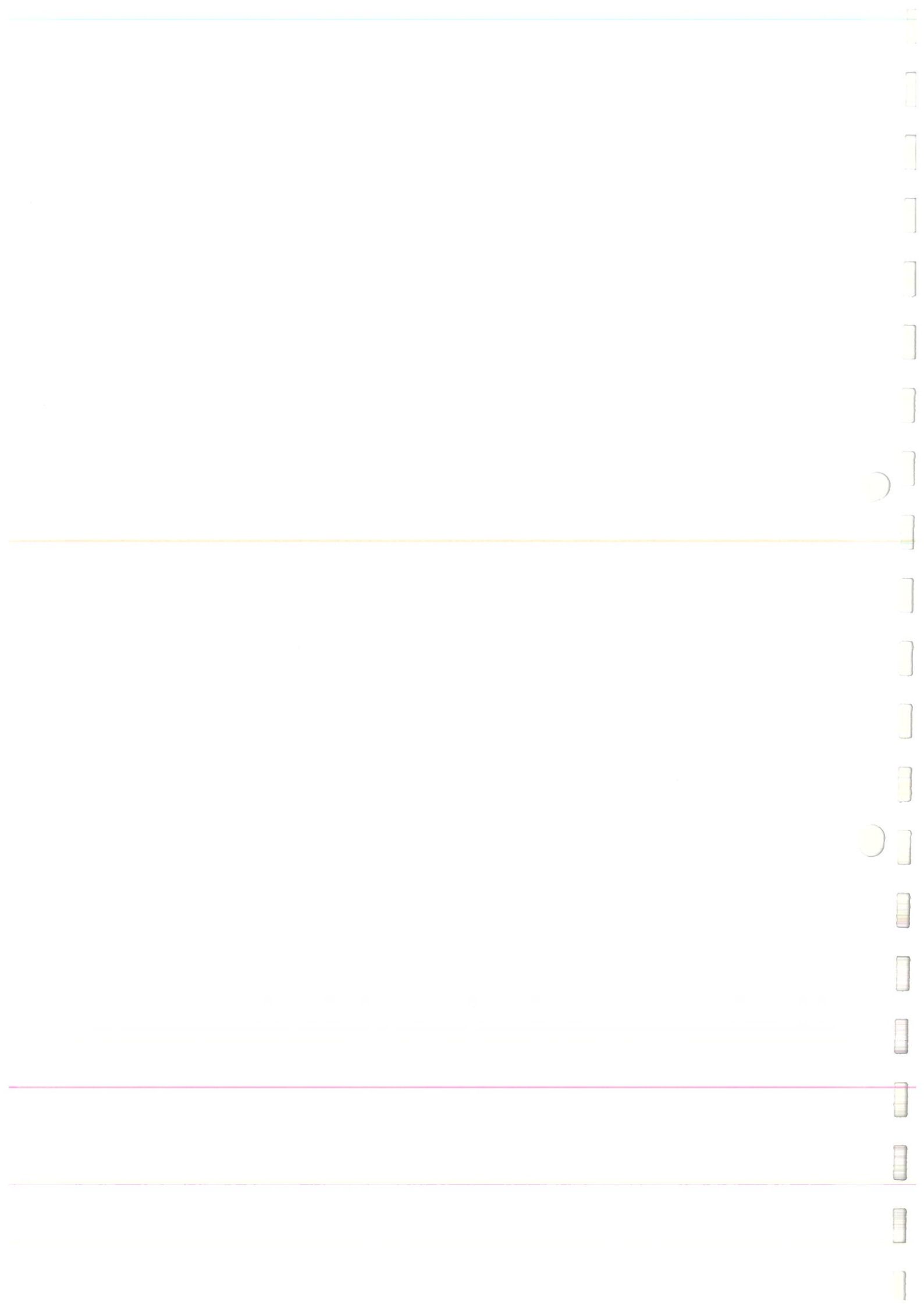
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# Solubility enhancement and application of cyclodextrins in local drug delivery

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## Abstract

Cyclodextrins (CDs) have been used in many pharmaceutical formulations as their constitution and inherent shape present advantages for drugs with poor aqueous solubility and low bioavailability. Because CDs can act as drug carriers by forming inclusion complexes to conjugate with many drugs, they have been applied in many drug delivery systems and can be used to develop new strategies. The objectives of this review are to describe the role of CDs in local administration, the ways in which CDs are used, and relevant studies currently underway. The basic structure and characteristics of CDs, as well as the mechanisms used to formulate inclusion complexes to solubilize drugs are also described. Several studies have been conducted to investigate the use of CDs and most have shown improvements in drug solubility and bioavailability. CDs show potential not only in the pharmaceutical industry but also in a variety of applications, and further research into the use of other drug carriers is therefore necessary.

**Keywords** Cyclodextrin · Inclusion complex · Local administration · Drug delivery · Drug carrier

## Introduction

Since the discovery of cyclodextrins (CDs) approximately 100 years ago, they have been used in several pharmaceutical industries (Vyas et al. 2008). Over 30 different pharmaceutical products using CDs are currently on the market (Table 1). The use of CDs improves the low solubility and bioavailability of drugs, facilitates absorption through the mucosa or skin, and enhances oral absorption (Baek et al. 2015; Kang et al. 2015). In addition, CDs have the advantage of preventing the rapid loss of drug, eliminating bitter taste, and allowing for a variety of formulations (Arima et al. 2001; Duchêne 1991; Loftsson et al. 2005).

CDs are cyclic oligosaccharides comprising ( $\alpha$ -1,4)-linked D-glucopyranose units and have a toroidal shape. Their outer surface is lipophilic and the inside is hydrophilic (Davis and Brewster 2004; Tiwari et al. 2010). The most common natural CDs used in the pharmaceutical industry are  $\alpha$ CD,  $\beta$ CD, and  $\gamma$ CD, consisting of 6, 7, and 8

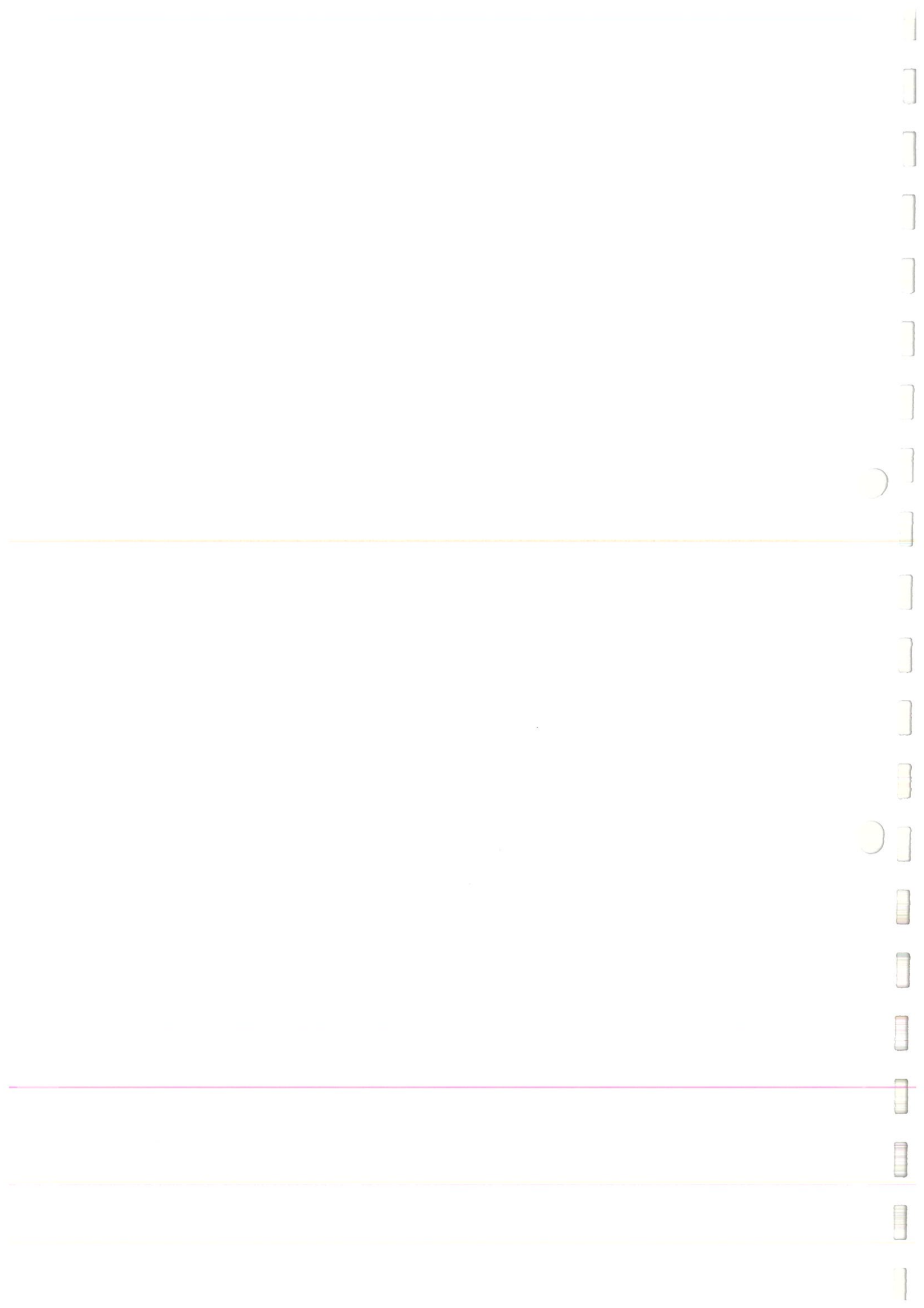
glucopyranose units, respectively (Shelley and Babu 2018). CDs react with various reagents such as trimethylamine and form derivatives that are more soluble in water than natural CDs. CD derivatives include hydroxypropylated CD (HP- $\beta$ CD and HP- $\gamma$ CD), carboxymethylated CD (CM- $\beta$ CD), and sulfobutylether CD (SBE- $\beta$ CD and SBE- $\gamma$ CD) (Loftsson and Duchêne 2007; Pinho et al. 2014). The features of natural CDs and CD derivatives are listed in Tables 2 and 3, respectively (Aqil et al. 2013; Davis and Brewster 2004; Jansook et al. 2018), and the three-dimensional structure is shown in Fig. 1.

CDs are used in many local drug delivery systems, including ophthalmic, nasal, pulmonary, buccal, vaginal, and rectal delivery (Choi et al. 2014; Kim et al. 2010). The advantages of local drug delivery include the reduction of first-pass and side effects, and increased effectiveness at relatively low doses (Baek et al. 2015). Easy administration also increases convenience for patients.

This review addressed the interactions and factors needed to form inclusion complexes when using CDs for drug solubilization. We also introduced the Higuchi and Connors method to analyze inclusion complex formed through solubilization and the pharmaceutical benefits that can be gained using CDs. In addition, the practical applications of CDs in

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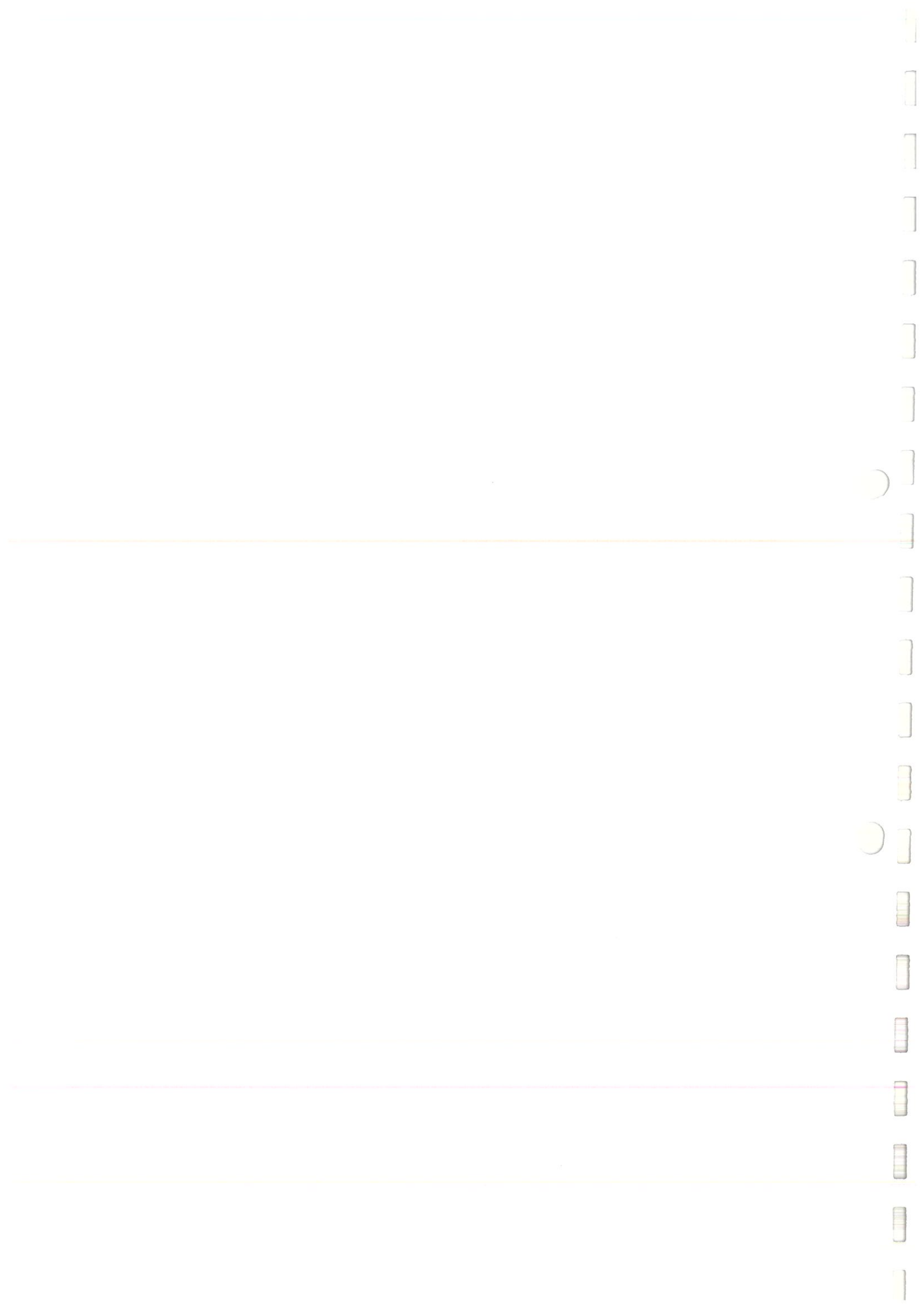
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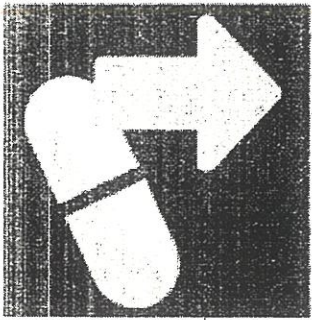




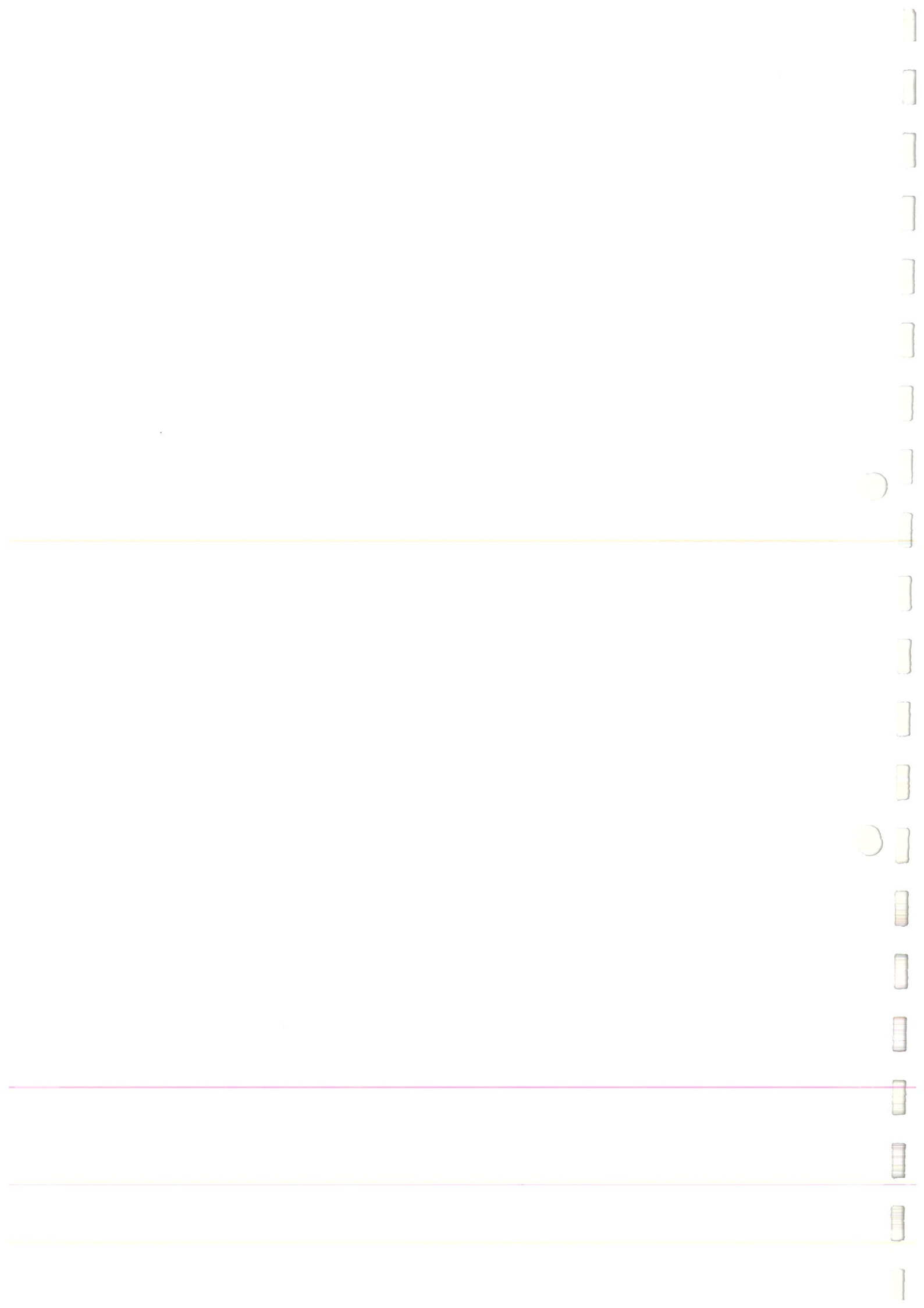
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Review

# Overview of the Manufacturing Methods of Solid Dispersion Technology for Improving the Solubility of Poorly Water-Soluble Drugs and Application to Anticancer Drugs

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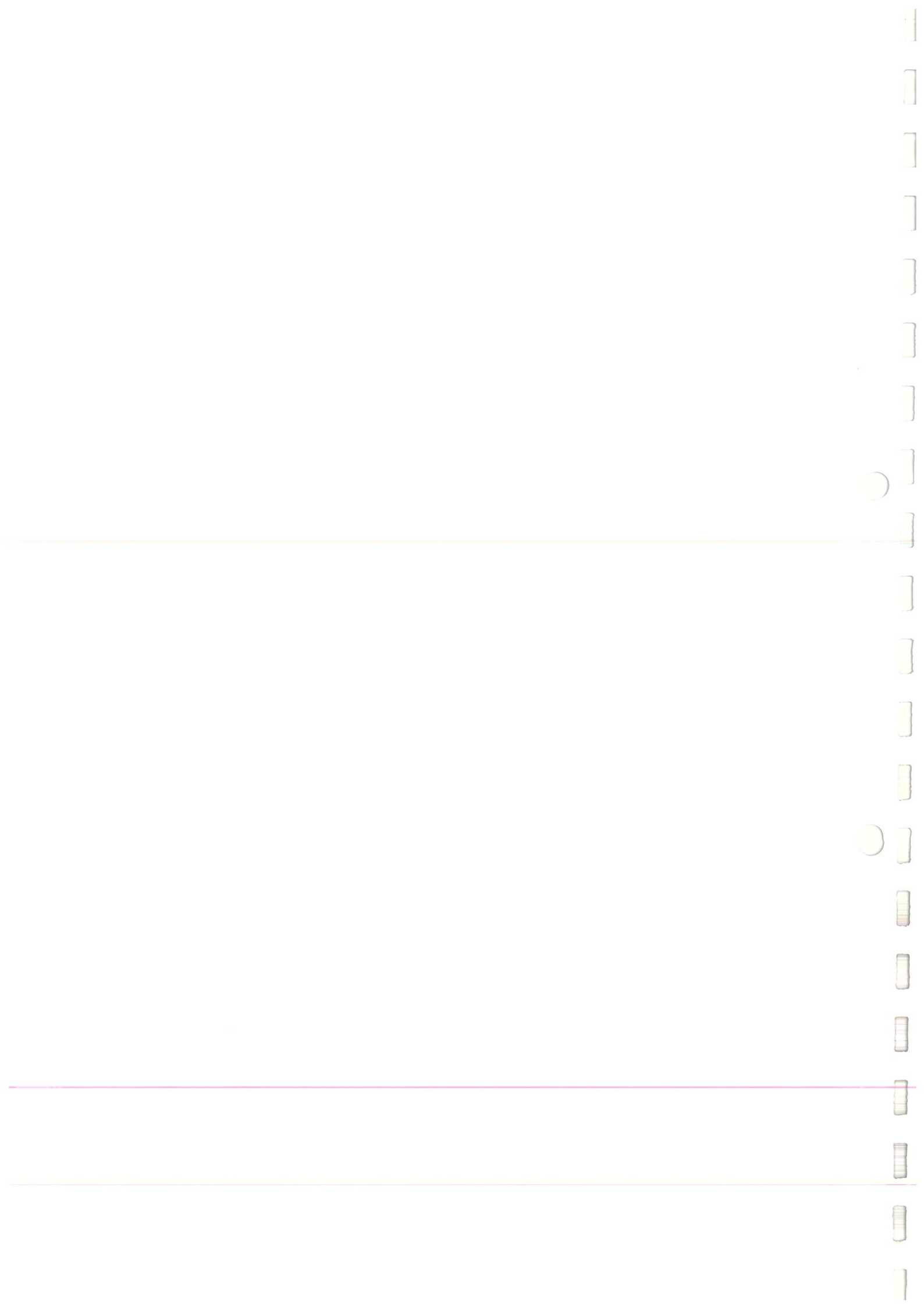


**Abstract:** Approximately 40% of new chemical entities (NCEs), including anticancer drugs, have been reported as poorly water-soluble compounds. Anticancer drugs are classified into biologic drugs (monoclonal antibodies) and small molecule drugs (nonbiologic anticancer drugs) based on effectiveness and safety profile. Biologic drugs are administered by intravenous (IV) injection due to their large molecular weight, while small molecule drugs are preferentially administered by gastrointestinal route. Even though IV injection is the fastest route of administration and ensures complete bioavailability, this route of administration causes patient inconvenience to visit a hospital for anticancer treatments. In addition, IV administration can cause several side effects such as severe hypersensitivity, myelosuppression, neutropenia, and neurotoxicity. Oral administration is the preferred route for drug delivery due to several advantages such as low cost, pain avoidance, and safety. The main problem of NCEs is a limited aqueous solubility, resulting in poor absorption and low bioavailability. Therefore, improving oral bioavailability of poorly water-soluble drugs is a great challenge in the development of pharmaceutical dosage forms. Several methods such as solid dispersion, complexation, lipid-based systems, micronization, nanonization, and co-crystals were developed to improve the solubility of hydrophobic drugs. Recently, solid dispersion is one of the most widely used and successful techniques in formulation development. This review mainly discusses classification, methods for preparation of solid dispersions, and use of solid dispersion for improving solubility of poorly soluble anticancer drugs.

**Keywords:** solid dispersion; classification; manufacturing methods; bioavailability; anticancer drugs

## 1. Introduction

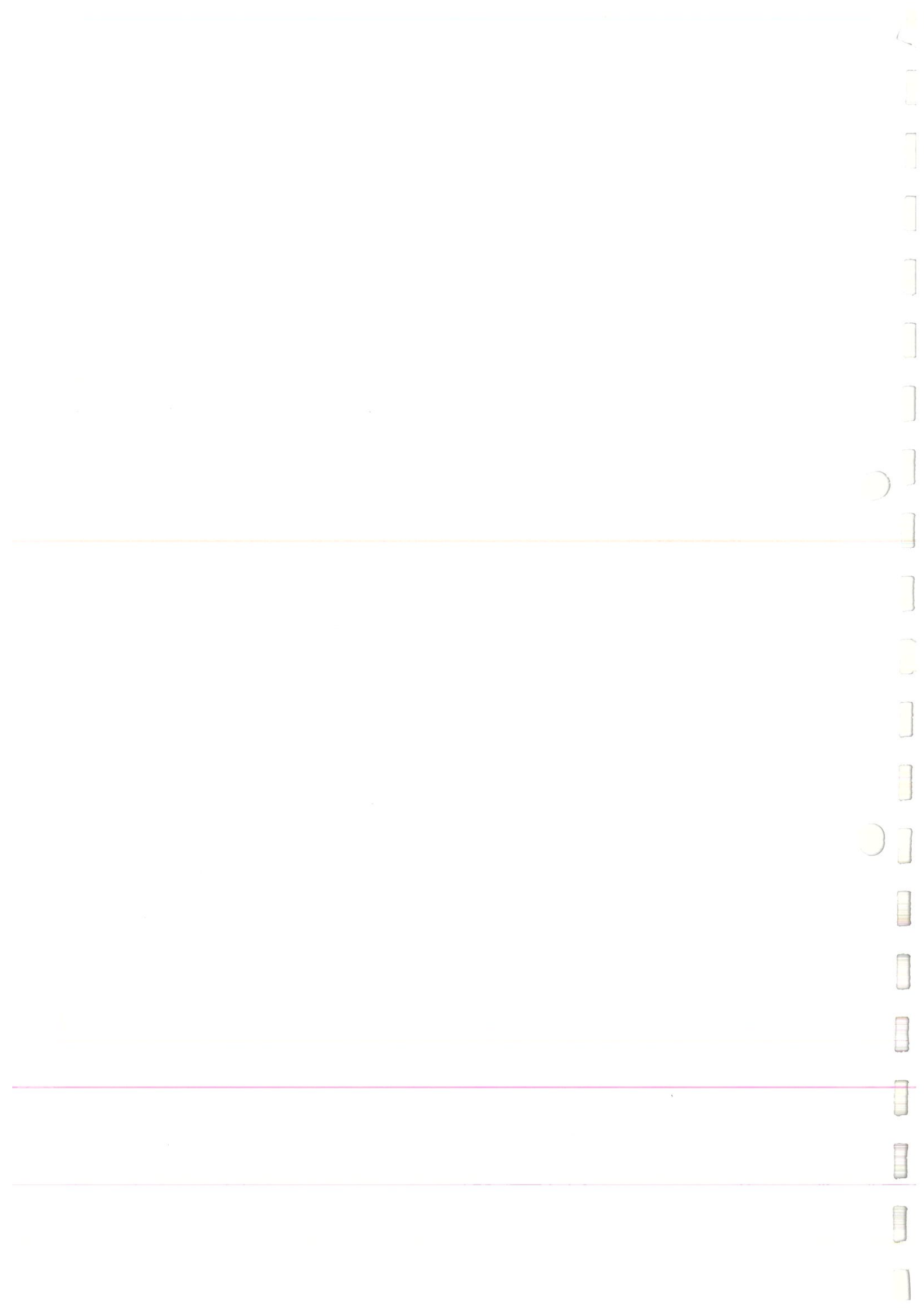
Cancer is one of the leading causes of death worldwide, and treatment remains a great challenge. Currently, there are three major cancer treatment strategies of surgery (performed by a surgical oncologist), chemotherapy (use of anticancer drugs), and radiotherapy (delivered by a radiooncologist) [1]. The objective of any treatment is to kill as many cancer cells as possible and minimize death of normal cells. Patients can receive monotherapy or combination therapy. For example, Hwang et al. [2] reported a combination of photodynamic therapy (PDT) and anti-tumor immunity



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## Using Case Teaching Methods Via Case Study - Factors Influencing FDI Capital in Vietnam

Dinh Nguyen An<sup>1</sup>

### Abstract

*Vietnam has experiences in using case study in teaching economic students at universities and colleges. In scientific language, there are many advantages of case teaching and including in case, the brightest, most prominent information such as: Results and Positive figures. For example in this paper we introduce a case of fast achievements in which Foreign Direct Investment (FDI capital) plays supporting roles for economic growth and social development.*

*One of this case study's purposes is to state What are effects of 5 macro variables on FDI and implications for policies. By using combination of quantitative methods and qualitative methods, our research results tell that : CPI, exchange rate and FDI have negative correlation whereas Trade balance, VNIndex and FDI have positive relation. So we would suggest government agencies, Ministry of Finance that: first, consider to reduce exchange rate ; second, consider to increase trade balance and VNIndex.*

*Therefore, our case study (method) can be expanded for other markets as well.*

**Keywords:** Case Teaching; Case Method; Teaching Quality; Vietnam; Policies.

**JEL:** A20, A2, A23, M21, G30.

### Introduction

First, When you study and research on a certain topic or field, the theory you learn is still only a theory, if it can't be applied to practice, the theories you learn will no longer make sense., which is a waste of time. That is to say, learning together with practice is effective, typically today's students, in addition to learning theory in school, in class, they also need to learn and practice by themselves to get Case Study yourself, then if you want, you can share it with others. Or, present-day teachers often have a Case Study attached to them when explaining a certain issue so

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that students can easily absorb and see that what they are learning can be applied in practice and from there, learning will become a reality. should be much more practical. With Case Study, learning will become more effective when apprenticeship can be paralleled with grasping theory as practical manipulation.

Next, we refer to below chart to see fluctuations of FDI, CPI and GDP growth in Vietnam over past years:

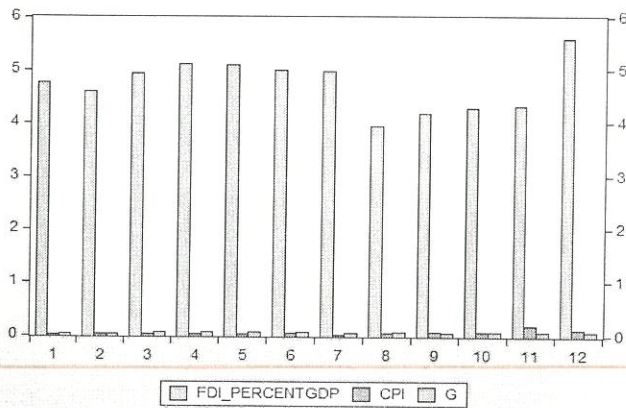


Chart 1. FDI movement

(source: author analysis with Eview)

The above chart shows us that movement of FDI flows as % GDP stable in 5 recent years.

**Research Questions**

Question 1: What are previous related studies?

Question 2: What are effects of 5 macro variables on FDI and implications for policies?

**Literature Review**

First, The results of case studies are often in the form of qualitative data (many words), so it can be difficult for the reader if the researcher’s writing ability is not good.

Case Study synthesizes situations, things, events, circumstances that go along with those things, phenomena and these things are real in reality. In it, you can use theoretical knowledge to begin to analyze, evaluate, and delve deeper into the inner problem. With Case Study with many people, you just need to see Case Study as practical examples to help make learning and finding practical experience more effective, which is the best way to understand Case Study.





In all topics and different fields, we can find suitable case studies. Even if you are just a student, you can still research and produce a Case Study that is relevant to your daily life. For example, you can build a case study that studies the brain's reaction when on the way to school you trip over a rock, fall and a bunch of other situations and from that infer the brain's response. Those are the case studies that are in practice, but to get them you also need to study, from which to experience and draw lessons.

Conventional story building is not enough, even if you have enough information and finished a case study. However, for a higher percentage of readers to become customers, you should still make the story compelling, exactly appealing to people who aren't part of your case study's audience.

A must-have story begins with background information that is the main subject of the case study.

Suddenly, one day, the subject encountered a serious problem that could not be solved.

That subject has solved the problem in a variety of ways, but with no success.

The object above keeps looking for a solution, until you show up.

With your products and services, you help the case study audience solve a problem.

You should detail your solution, but don't reveal all the secrets.

You end the story by stating the subject's subsequent results.

Then, We summarize previous studies as follows:

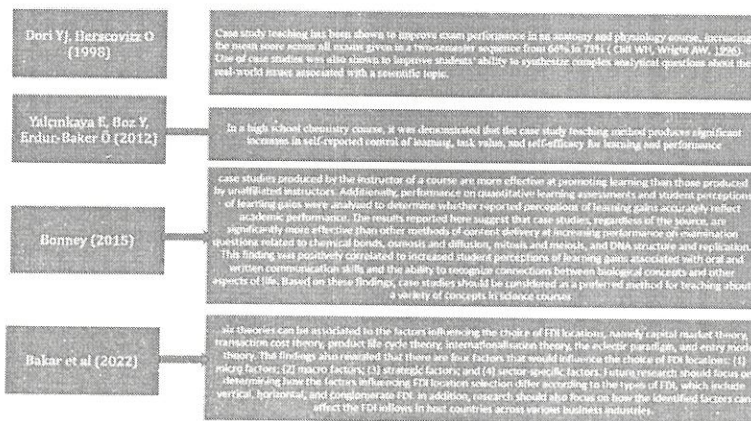


Figure 1. Summary of Previous Studies

(Source: Author Synthesis)



## Methodology

### *Method and Data*

This study mainly use combination of quantitative methods and qualitative methods including synthesis, inductive and explanatory methods.

*Case Study Method is Introduced with Example case.*

## Main Findings

### *1. A Case Study Example*

In below section we present case study example:

**Case Title: Factors Influencing FDI Capital in Vietnam**

**Step 1: Case background introduction**

**Step 2: Case contents**

**Step 3: Case data**

**Step 4: Case questions**

**Step 5: Case discussion**

### *Conclusion*

#### *First we Understand Background (Step 1)*

After more than 30 years of opening up to attract investment, FDI capital has been and still plays a very important role in socio-economic development. And in fact, over the years, the rate of foreign investment in Vietnam has continuously increased, the investment activities of investors in Vietnam have not decreased in terms of excitement, efficiency and quality.

According to experts and state management agencies, foreign direct investment (FDI) is a particularly important capital flow for growth and international economic integration, contributing to supplementing capital, technology, and capacity. management, business ability, ability to organize and participate in the global supply chain. After more than 30 years of opening up to attract investment, FDI capital has been and still plays a very important role in socio-economic development. The growth of foreign investment capital not only creates many favorable conditions for Vietnam to accelerate the time of international market expansion, but also improves in many aspects in business activities (expertise, technology, engineering...), reducing the burden of capital for many large projects.





In addition, the attraction and use of foreign capital also contributes to promoting economic transformation and restructuring, renovating the growth model, and improving the competitiveness of the country, industry and product. products and services; promote institutional reform, legal policies, business environment, develop a fully, modern and integrated market economy.

Recognizing the significance and role of FDI in Vietnam, the Vietnamese Government has issued many policies and implemented many solutions to create an attractive and safe investment environment. Enterprises themselves are also constantly improving in terms of human resources and production lines to attract investors. In response to those efforts, over the years, the rate of foreign investment in Vietnam has continuously grown, and even when the world was significantly impacted by the COVID-19 pandemic, the investment activities of foreign investors in Vietnam have continued to grow. Investment in Vietnam has not decreased in terms of excitement, efficiency and quality.

(source ictvietnam.vn)

*Look at Below Charts we Found Out*

- There are negative corr between: FDI and ex rate (chart 3), FDI and CPI (chart 4).
- While there are positive corr between: FDI and trade balance (chart 2).

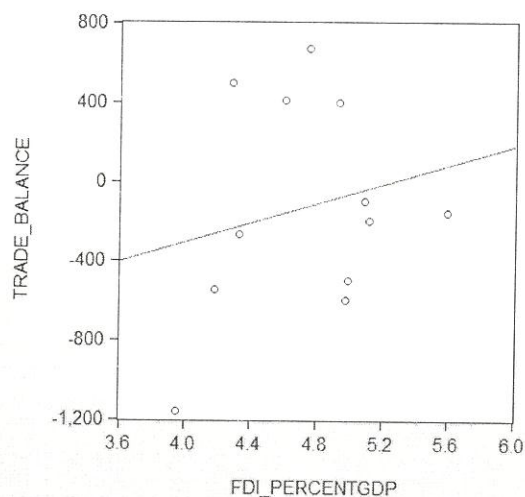


Chart 2. FDI and Trade Balance



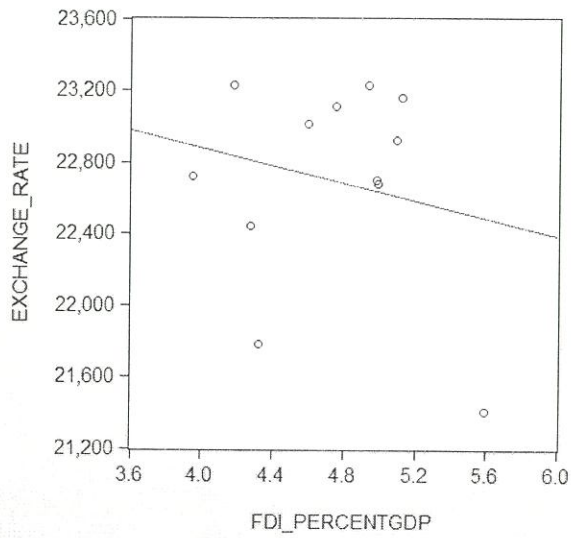


Chart 3. FDI and Exchange Rate

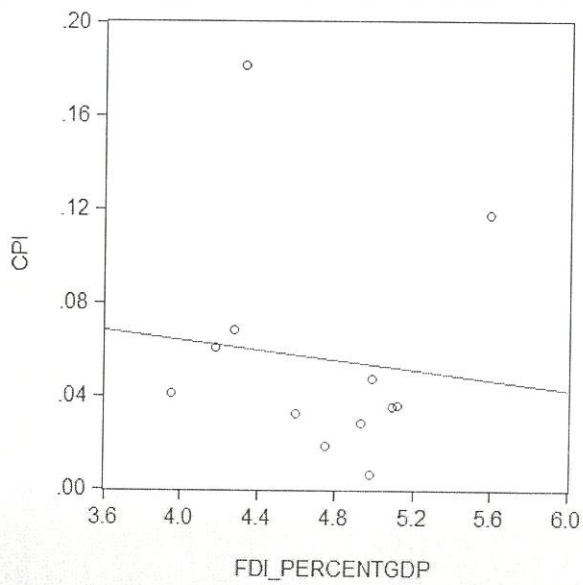


Chart 4. FDI and CPI

(source: author analysis with Eview)





**Regression Results**

**Fig 1 - Regression for 4-5 Variables**

We see below table.

	4 variables - coefficient	5 variables – coefficient
G	10.07	18.4
CPI	-8.04	-5.5
Exchange rate	-0.0007	-0.0008
Trade balance	0.0003	5.90E
VNIndex		0.001
C	20.6	23.2
R-squared	0.39	0.6
SER	0.46	0.4

*(source: author analysis with Eview)*

**Then Next Step: In Classrooms, We Discuss Case Questions for Students**

*Question 1: What are roles of FDI?*

*Question 2: What are impacts of factors on FDI?*

**Case Discussion**

In reality, not only FDI helps to increase GDP growth and increase national budget, but it also increase the number of jobs and train high-quality workers. Expanding the consumption market entails a large scale of production; improve production, reduce product costs in line with consumers' incomes.

Currently, Vietnam has been removed from the list of underdeveloped economies and into the group of middle-income countries. However, there are still different views when assessing the role of FDI in the economy. There is an opinion that FDI plays an important role, helping to develop a strong economy, but there is also another opinion that the more FDI is attracted, the more losses (damage from environmental pollution caused by FDI, losses). due to transfer pricing, paying cheap labor for Vietnamese human resources...).

The total benefits brought by FDI and the loss of value caused by FDI have also not been calculated. In that context, the author conducts research on the economic efficiency of FDI, the role of FDI in Vietnam's economy and recommends solutions to be taken to promote the role of FDI in the coming years.



Besides the positive effects, the process of attracting and operating the FDI sector also appears to have negative effects on the economy of the country attracting FDI. In which, can be mentioned such as: Causing environmental pollution because of avoiding construction of waste treatment works; Tax evasion through declaration of "false losses and real gains" causes damage to the economy of the country attracting FDI; Through transfer pricing to realize "fake loss and real gain", loss of revenue of the country attracting FDI; It is possible to evade responsibility for employees through failure to implement social insurance regimes and ignore the rightful rights of employees according to the law of FDI attraction countries.

Rubio (2021) presents a comprehensive analysis of the relationship between FDI and growth for a particular country, which seems to be a more promising empirical approach rather than the approach based on panel regressions, where sometimes some dissimilar experiences are added together.

#### *Next We See During the Research Period 2010-2021*

Results from above regression table show us that: CPI and exchange rate reduce will cause FDI increase, and GDP growth increase will cause FDI increase. Because Results from above regression table show us that: CPI and exchange rate reduce will cause FDI increase, and GDP growth increase will cause FDI increase. Moreover, Trade balance and VNIndex decrease will cause FDI decline.

So we would suggest government agencies, Ministry of Finance that:

- Consider to reduce exchange rate.
- Consider to increase trade balance and VnIndex.

#### **Conclusion**

##### *Using Case Teaching Methods and Implications*

The essence of a case study is to elucidate a decision or establish decisions: why they were made, how they were done, and with what results (Schramm, 1971). The above definition refers to the case study of decisions that are the main focus of the case study method. However, there are other common case studies, such as individuals, organizations, processes, programs, or even programs. events (events), etc.

Last but not least we see figure:





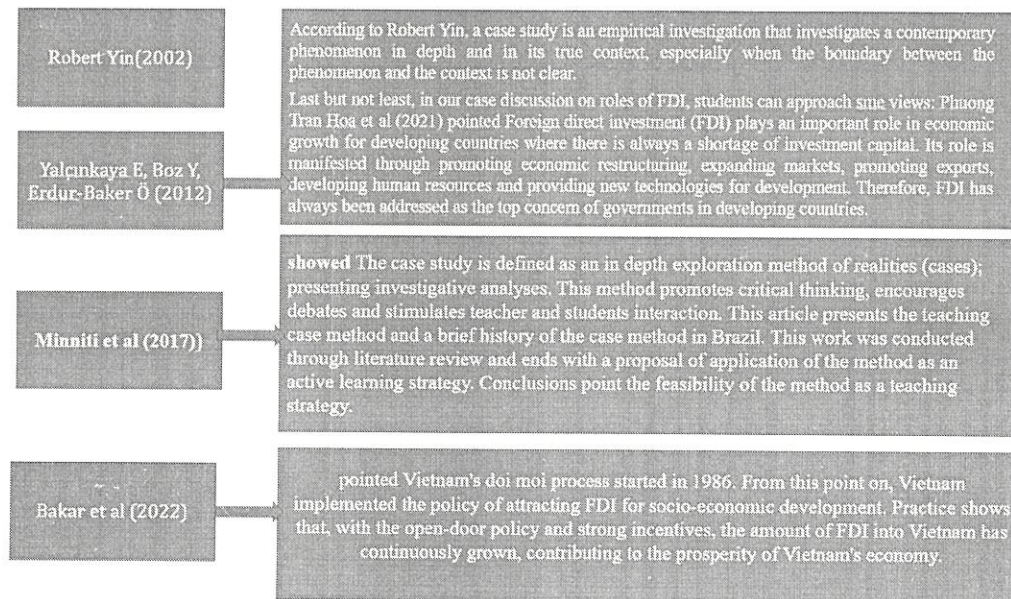


Figure 2. Values of Case Study

(source: author analysis and synthesis)

### Limitation of Research

We can expand our research model for other markets.

### Conflicts of Interest

There is no conflict of interest.

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