An overview of Nano fibre membranes to deliver natural ingredient or extract for targeted drug-delivery devices

Sukhwinder K. Bhullar[1,2]

[1]Department of Mechanical Engineering, Bursa Technical University, Bursa, Turkey

[2]Department of Mechanical Engineering, University of Victoria, Victoria, BC, Canada

Abstract

Herbal based medicines are used for the treatment of many diseases from ancient times while pharmaceutical chemistry is recently developed. Usually Herbal medicines have been delivered orally in both animals and human. Targeted drug-delivery systems currently more common for the treatment of most life threatening diseases such as cancers. In addition to drug eluting devices many nano based devices delivering active pharmaceutical ingredients or herbal based extracts or particles are growing in demand and they have been approved by FDA and other regulatory bodies. This mini review intends to overview role of nanofibers for the delivery of herbal ingredients and natural plant based extract for the biomedical applications.

INTRODUCTION

Natural products have been used for the treatment of both human and animals diseases since ancient time in India, ancient China, Egypt, Africa and America. Pharmaceutical chemistry and chemical analysis developed in the early 19th century and they started the extraction and modification of herbal ingredients including plant based natural extracts [1-2]. Today herbal medicines in their novel formulations such as nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes and SLNs, nanomicellar system, nanotubes, and colloidal nanogels have been developed to be used alone as well as in combination with other chemotherapeutic agents [1,3-4]. In addition, the current focus of pharmaceutical researchers is towards design, characterization and development of targeted drug delivery systems for herbal medicines to enhance their effect, response and deliver require quantity of drug to targeted diseased area [5-11]. The challenges with herbal drugs delivery such as smashing of some constitutes of herbal drugs in the highly acidic pH of the stomach and metabolization of some constituents by liver prevent the optimum quantity of the herbal drugs to reach the blood [1,12]. Nano Carriers promote their candidature for herbal remedies to deliver required amount of herbal drugs to targeted diseased area overcoming all the obstacles related to deliver their optimum quantity due to their small size and increased surface area. Sharma et al reported [1] that novel nano drug delivery systems for herbal remedies offer (i) reduction in bulk doses; (ii) delivery at the targeted diseased area for major life threatening diseases;(iii) ease and comfort to patients over the traditional available formulation such as large doses but less effective; (iv)ability to deliver high concentrations of drugs to disease sites due to their unique size and high loading capacities and persist at the sites for the longer periods; (v)

enhanced permeation and retention effect; (vi) reduces side effects and (vii) reduction in the dose of the drug formulation. Due to significant results nanomaterials and nanotechnology FDA and other drug regulatory bodies have approved many nanoparticles and nanofibers based devices to deliver active pharmaceutical ingredients. There is growing demand for further research to exploit benefits of these devices to enhance their benefits to improve the quality of life of patients. Nano fibre membranes offer their potentials for drug incorporation and drug release. Here, the main focus of this review is to present nanofibrous herbal drug delivery systems.

HERBAL DRUG DELIVERY SYSTEMS AND NANOTECHNOLOGY

Over the last decades the application of nanomaterial and nanotechnology have been growing interest in pharmaceuticals in both synthetic and herbal medicines. Ultra small size materials in 1-100nm range have unique physiochemical properties and interactions with biological systems while nanotechnology helps in understanding and control these nano materials [13]. For drug loading a variety of ways are used to laod drugs in nanoparticale and nano fibers such as non woven structures, absorption and chemical conjugation. The advantages of nanoparticle based drug delivery such as improving serum solubility of the drugs, prolonging the systemic circulation lifetime, releasing drugs at a sustained and controlled manner, preferentially delivering drugs to the tissues and cells. Also, concurrently delivery of multiple therapeutic agents to the same cells for combination therapy are reported by the authors in [14-15]. In addition, they discussed that the pharmacokinetics and therapeutic index of the drugs can be significantly improved in contrast to the free drug counterparts as drug-loaded nanoparticles can enter host cells through endocytosis and then release drug payloads to treat microbes-induced intracellular infections. Having negligible side effects compared to synthetic medicines and awareness of physicians and patients for their benefits, herbal medicines have been used globally. To increase the therapeutic values, bioavailability and for the treatment of chronic diseases like asthma, diabetes, cancer, other life threatening and common diseases herbal nano drug delivery systems can be fabricated with biomaterials such as synthetic biodegradable polymers, lipids, and polysaccharides [16]. Some of herbal based drug delivery systems are given in **Table 1**.

Table 1 Herbal based drug delivery systems

Drug Delivery system	Procedure	Herbals	Biomedical Applications	Ref.
Mouth dissolving tablets	poly-herbal		effective for lung problems and other respiratory ailments like asthma , cardiac distress	[17]
Matrix tablets or in multi-particulate formulations like microcapsules	a granulated herb and a carrier	*active ingredients from the group consisting of hypericin, hyperforin and echinacosides*	steady supply of the active components for a sustained period for the treatment of targeted drug delivery to control diseases	[18]

Microgranules	extrusion-spheronization, fluid air bed process or a coating-pan method	*Gingko Biloba*	Particularly to supply mixtures of plant extracts to cure diseases	[19]
Mucoadhesive system	muco-adhesive polymers	*Echinacea, Lavender and Mastic gum*	sustained release for the treatment of diseases	[20]
Transdermal films	transdermal drug delivery system (TDDS)	*Boswellic acid (Boswellia serrata) and curcumin (Curcuma longa)*	for continuous drug administration through skin into the systemic circulation and avoids the first pass metabolism of the drug without the pain associated with injection; offers drug delivery with infrequent dosing via zero-order kinetics; and the therapy can be easily terminated at any time.	[21]
Herbal-based oral composition for periodic retention within the buccal cavity of a human	the group consisting of gels, pastes and chewing gums.	*Radix Polygoni Multiflori, Rhizoma Drynariae, Rhizoma Ligustici Chuanxiong, Calculus Bovis, Indigo Naturalis, Herba Ecliptae, Pericarpium Trichosanthis, Radix Sophorae Flavescentis, Spina Gleditsiae, Radix Angelicae Sinensis, Fructus Mori and Halitum.*	to reduce loss of scalp hair and to promote hair growth	[22]
Shuanghuanglian aerosol (SHLA)	Flos Chrysanthemum Indicum, Flos Lonicera, Herba Houttuynia, Radix Bupleurum and menthene	*Flos Lonicera, Fructus Forsythia and Radix Scutellaria.*	Anti-inflammatory and antiviral effects; a good curative effect in treating infantile upper respiratory tract infections.	[23]
Microparticles	formulated by different techniques using chitosan, egg	*Gugulipid extract from the oleo gum resin of Commiphora*	to reduce the levels of harmful serum lipids in the blood stream.	[24]

	albumin, sodium alginate, ethyl cellulose, cellulose acetate, gelatin and beeswax.	*wightii*		
Microcapsules	layer-by-layer adsorption of carrageenan and oligochitosan onto calcium carbonate microparticles with their subsequent dissolving after the treatment of EDTA.	*plantain Plantago major and calendula Calendula officinalis L. (PCE)*	to accelerates gastric tissue repair	[25]
Nanoparticles of TCH (traditional Chinese herbs)	drying, mincing, extracting, crushing into liquid particles with ultrasonic wave, filtering and nanometerizing into nanoparticles soliquid with nanometer collider.	*peach seed, safflower, angelica root, Szechwan lovage rhizome, Rehmannia root, red peony root, leech, gadfly, earth worm and ground beetle,*	for quick recovery from arterial embolism and diminution of thrombi	[26]
Sustained-release implant	Chitosan	*danshen (Radix Salvia miltiorrhiza),*	To promote anastomosing and healing on muscles and tissues at the organic incision site in abdominal cavities.	[27]
ArthriBlend-SR	formulation containing herbal extracts and nutrients	*Glucosamine sulfate, Boswellin (Boswellia serrata extract) and Curcumin C3 Complex (Curcuminoids from Curcuma longa)*	to support healthy joints and connective tissues in the body; natural actives for joint care applications; to support the management of inflammatory conditions such as arthritis and the continuous management of symptoms of arthritis	[28]

Nanofibers of both biopolymers and synthetic polymers have been successfully fabricated [29] which offer high porosity with large surface area-to-volume ratio and are more appropriate for cell accommodation, nutrition infiltration, gas exchange and waste excretion [30]. Use of herbals including plant extracts, powder and nanoparticles for biomedical applications blended with polymers in form of films or nano/microfibers form is growing interest of researchers due to their biomedical applications. Most of work in literature as illustrated in **Table**

2, is reported by authors in [31-34] for different herbals blended nanofibrous mats with Polycaptolactone (PCL) due to its biocompatibility, biodegradability and good drug permeability for wound healing dressing , targeted drug delivery systems and skin tissue engineering.

Table 2 Herbals blended with polymers

Polymer (Nanofibers)	**Solvents**	**Herbals**	**Biomedical applications**	**Ref.**
PCL/PVP	Chloroform/ methanol	*crude bark extract of Tecomella undulata,*	wound healing and wound dressing	[31]
PCL	chloroform	*aloe vera*	Wound dressing applications	[31]
Gelatin powder	Butanol, dichloromethane, hexane and methanol	*Extraction of Centella asiatica*	wound healing ability	[32]
PCL	Dichloromethane (DCM) and N,N-dimethylformamide (DMF)	*Shikonin*	treatment of wound healing and/or atopic dermatitis	[33]
PCL	chloroform/ methanol	*Indigofera aspalathoides, Azadirachta indica, Memecylon edule (ME) and Myristica andamanica*	skin tissue engineering	[34]

Conclusion

This review summarizes the most recent development of polymeric herbals incorporated drug delivery system and nanofibers loaded with natural extract. These nano to macro structure promote their candidatures for biomedical applications for wound healing and for the treatment of many other diseases to improve quality of life of patients. A very limited work is done in fabrication and characterztion of polymer-herbal blended nanofibers. More work is needed to be done with different biocompatible polymer nanofibers loaded with herbal extracts in their nanoform and exploit their benefits using combination multidisciplinary approach and interdisciplinary research.

References

1. Sharma AT, Mitkare SS, Moon RS. Multicomponent herbal therapy: A review. Int J Pharm Sci Rev Res. 2011;6:185–7.
2. Patwardhan B, Vaidya AD, Chorghade M. Ayurveda and natural products drug discovery. Curr Sci. 2004;86:789.
3. Bisht S, Feldmann G, Soni S, Ravi R, Karikar C, Maitra A, et al. Polymeric

nanoparticle-encapsulated curcumin ("nanocurcumin"): A novel strategy for human cancer therapy. J Nanobio. 2007;5:1–18.
4. Zheng L, Song JF. Curcumin multi-wall carbon nanotubes modified glassy carbon electrode and its electrocatalytic activity towards oxidation of hydrazine. Sens Actuators B Chem. 2009;135:650–5.
5. Yen FL, Wu TH, Lin GT, Cham TM, Lin CC. Nanoparticles formulation of Cuscuta chinensis prevents acetaminophen-induced hepatotoxicity in rats. Food Chem Toxicol. 2008;46:1771–7.
6. Zhang JF, Hou SX, Liu HL. Comparison of preparing two polylactide nanoparticles loaded lipophilic anti-cancer herb drug by nanoprecipitation method. Zhongguo Zhong Yao Za Zhi. 2007;32:303–6.
7. Li Y, Dong L, Jia A, Chang X, Xue H. Preparation and characterization of solid lipid nanoparticles loaded traditional chinese medicine. Int J Biol Macromol. 2006;38:296–9.
8. Robinson JR. Introduction: semi-solid formulations for oral drug delivery. Bull Tech Gattefosse. 1996;89:11–3.
9. Aungst BJ. Novel formulation strategies for improving oral bioavailability of drugs with poor membrane permeation or presystemic metabolism. J Pharm Sci. 1993;82:979–87. DeMario MD, Ratain MJ. Oral chemotherapy: rationale and future directions. J Clin Oncol. 1998;16:2557–67.
10. Pouton CW. Formulation of self-emulsifying drug delivery systems. Adv Drug Del Rev. 1997;25:47–58.
11. Bairwa NK, Sethiya NK, Mishra SH. Protective effect of stem bark of Ceiba pentandra Linn. against Paracetamol-induced hepatotoxicity in Rats. Pharmacognosy Res. 2010;2:26–30.
12. Zhang, L.; Gu, F. X.; Chan, J. M.; Wang, A. Z.; Langer, R. S.; Farokhzad, O. C. Nanoparticles in medicine: therapeutic applications and developments. Clin. Pharmacol. Ther. 2008, 83, 761-9.
13. Davis, M. E.; Chen, Z. G.; Shin, D. M. Nanoparticle therapeutics: an emerging treatment modality for cancer. Nat Rev Drug Discov 2008, 7, 771-82.
14. Peer, D.; Karp, J. M.; Hong, S.; Farokhzad, O. C.; Margalit, R.;Langer, R. Nanocarriers as an emerging platform for cancer therapy. Nat Nanotechnol 2007, 2, 751-60.
15. S. H. Ansari, Farha Islam, and Mohd. Sameem, Influence of nanotechnology on herbal drugs: A Review, J Adv Pharm Technol Res. 2012 Jul-Sep; 3(3): 142–146. doi: 10.4103/2231-4040.101006.
16. Parakh SR, Gothoskar AV. Review of mouth dissolving tablet technologies.Pharmaceutical Technology. Advanstar Communications, Duluth, MN, ETATS-UNIS. 2003:47–52.
17. Blatt Y, Kimmelman E, Cohen D, Rotman A. Microencapsulated and controlled-release herbal formulations. United States Patent 6340478.
18. Marechal D, Yang Wg, Yuzhang H. Sustained-release microgranules containing gingko biloba extract and the process for manufacturing these. United States Patent 7569236.
19. Sterer N, Nuas S, Mizrahi B, Goldenberg C, Weiss EI, Domb A, et al. Oral malodor reduction by a palatal mucoadhesive tablet containing herbal formulation. J Dent. 2008; 36:535–9.
20. Verma M, Gupta PK, Varsha BP, Purohit AP. Development of transdermal drug dosage formulation for the anti-rheumatic ayurvedic medicinal plants. Ancient Sci Life,2007;1 :66–9.
21. Chung H, Burk H, Shu K. Herbal-based oral composition and process for producing the same. 2001 European Patent EP0862446.
22. Ma B, Duan X, Wang Z. Clinical and experimental study on Shuanghua aerosol in

treating infantile upper respiratory tract infection. Zhongguo Zhong Xi Yi Jie He Za Zhi. 2000;20:653–5.
23. Tanwar YS, Gupta GD, Ramawa KG. The Pharma Review. New Delhi: Kongposh Publications Pvt. Ltd; 2006. Development and evaluation of microparticles of Gugulipid; pp. 124–32.
24. Borodina TN, Rumsh LD, Kunizhev SM, Sukhorukov GB, Vorozhtsov GN, Feldman BM, et al. Entrapment of herbal extracts into biodegradable microcapsules. Biochem Suppl Series B Biomed Chem. 2008;2:176–82.
25. Shen YJ, Zhang ZW, Luo XG, Wang XF, Wang HL. Nanoparticles of traditional chinese herbs inhibit thrombosis in vivo.Haematologica. Heamatol Jr. 2008;93:J1457.
26. Zhao HR, Wang K, Zhao Y, Pan LQ. Novel sustained-release implant of herb extract using chitosan. Biomaterials. 2002; 23:4459–62.
27. ArthriBlend SR. A formulation containing herbal extracts and nutrients to support healthy joints and connective tissues in the body. Nutraceuticals World. 2009 Nov 05. Available from: http://findarticles.com/particles/mi_hb223/is_6_7/ai_n29102045/
28. E. Luong-Van, L Grondahl, K. N. Chua, K. W. Leong, V. Nurcombe, and S. M. Cool, "Controlled release of heparin from poly(ε-aprolactone) electrospun fibers," Biomaterials, 2006, vol. 27, 2042–2050.
29. Z. M. Huang, Y. Z. Zhang, M. Kotaki, and S. Ramakrishna, "A review on polymer nanofibers by electrospinning and their applications in nanocomposites," Composites Sci. Technol., 2003, vol. 63 , pp. 2223–2253.
30. Guorui Jin , Molamma P. Prabhakaran b, Dan Kai, Sathesh Kumar Annamalai, Kantha D. Arunachalam , Seeram Ramakrishna, Tissue engineered plant extracts as nanofibrous wound dressing, Biomaterials 34,2013, 724-734.
31. S. Suganya, T. Senthil Ram, B. S. Lakshmi, V. R. Giridev, Herbal Drug Incorporated Antibacterial Nanofibrous Mat Fabricated by Electrospinning: An Excellent Matrix For Wound Dressings, Journal ofApplied Polymer Science,Vol. 121, 2893–2899, 2011, VC 2011 Wiley Periodicals, Inc.
32. Panprung Sikareepaisan, Apichart Suksamrarn and Pitt Supaphol, Electrospun gelatin fiber mats containing a herbal—Centella asiatica—extract and release characteristic of asiaticoside, Nanotechnology 19, 2008, doi:10.1088/0957-4484/19/01/015102.
33. Jie Han, Hai-Tao Zhang, Li-Min Zhu, Christopher J Branford-White, Electrospun biodegradable nanofiber mats for controlled release of herbal medicine 978-1-4244-2902-2009 IEEE
34. S. Agnes Mary and V.R. Giri Dev, Electrospun herbal nanofibrous wound dressings for skin tissue engineering, The Journal of The Textile Institute, 2015, Vol. 106, No. 8, 886–895, http://dx.doi.org/10.1080/00405000.2014.951247.