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Mechanochemical-assisted extraction method on Medicinal plants: A Brief Review

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ABSTRACT

Background: Extraction method in medicinal plants is one of major issue in isolation of bioactive compounds. Mechanochemical-assisted extraction method (MCAE) is one of useful method of extraction. **Objective:** This paper will review the use of MCAE in medicinal plants, method of preparation of sample, experimental design for optimization procedure. **Results:** Mechanochemical-assisted extraction method is especially useful for poorly water-soluble components because of eco-friendly nature, extreme fine grinding, decrease in processing time, lower extraction temperature and minimizing the cost. It helps to decrease the use of organic solvents and targeting the bioactive compounds by avoiding the chlorophyll content to leach inside the sample. **Conclusion:** Mechanochemical assisted extraction can create a substantial impact to ecofriendly processing of medicinal plants.

KEYWORDS: Mechanochemical-assisted extraction, Medicinal plants, Extraction of bioactive compounds

INTRODUCTION

Plants are an important source of medicine. Life without plants cannot be possible [1]. There is an increased in study of Medicinal plants due to its ability to treat common and uncommon disease with scientific proofs. Extraction method plays an important role to identify bioactive compounds [2]. An extensive variety of extraction procedure is available nowadays. From the last decade, scientists are trying to find new ways to extract bioactive compounds. Among them, Mechanochemical-assisted extraction method (MCAE) belongs to newly selected area of research to target bioactive compounds in an easy and faster way. In this paper our focus is to identify the literature on previous methodologies, experimental design using Mechanochemical-assisted extraction on medicinal plants. This literature will provide an assistance to understand the readers about previous experimental design and helps to adopt on other medicinal plants.

Medicinal plants in Mechanochemical-assisted extraction method:

Salvia miltiorrhiza, commonly famous for its medicinal use in traditional Chinese medicine belongs to genus Saliva [3]. Different Extraction techniques was applied in *Salvia miltiorrhiza* such as microwave-assisted extraction (MAE), extraction at room temperature (ERT), heat reflux extraction, ultrasonic extraction and Soxhlet extraction. Among them microwave extraction was the most effective technique but the cost of energy consumption is too high which make it less viable for large scale extraction. Secondly, it was less effective for targeted biomolecules. Particle size was one of an important factor in microwave extraction where as in MCAE process had an advantage due to very fine particle size [4][5]. *Camellia oleifera* Abel commonly known as tea oil is widely distributed in China [6]. *Eleutherococcus senticosus* is commonly known as Siberian ginseng. It was found to have multiple medicinal uses such as anti-microbial, anti-viral, immunomodulatory effect and anti-oxidant [7]. *Sophora flavescens* belongs to family Fabiaceae. It possess many health benefits such as chronic inflammatory disorders and Anti-atherosclerosis [8][9]. *Magnolia officinalis* native to China belongs to family Magnoliaceae and is known for magnolol and honokiol, two polyphenolic compounds used in treatment of dermatological disorder [10]. There are several other medicinal plants enlist in MCAE as mentioned in table 1.

Table 1: List of plant material involved in Mechanochemical-assisted extraction method

List of Plant Material	Solvents	Instrumentation	Solid reagents	Statistical Design	Targeted Bioactive Compounds	Pharmacological activity	Result	Reference
Salvia Miltiorrhiza Bunge	Ionic Liquid	Ball mill (FastPrep®-24, MP Biomedicals LLC, USA)	Mixed with ionic liquid and then extracted with Ball mill	Response Surface Methodology (RSM) by Box-Behnken Design (BBD)	Tanshinones	n.a.	A	[11]
Camellia oleifera Abel. Meal	Water	AGO-2 high-intensity planetary activator	NaOH	Response Surface Methodology (RSM) by Central composite Design (CCD)	Kaempferol glycosides	Anti-oxidant	B	[12]
Eleutherococcus senticosus roots and rhizome	Water	Energy-intensive vibrational mill (model WZJ(BFM)-6J; Billionpowder Tech & Engineering Co., Ltd., Jinan, China	Na_2CO_3	One-way ANOVA with the Student-Neuman-Keuls (SNK) test for multiple comparison	Isofraxidin	n.a.	C	[13]
Sophora flavescens Root	Water	PM-200 planetary mill, Retsch, Haan, Germany	Solid reagent (Sodium borate, diatomaceous earth, basic aluminum oxide, Ca_2CO_3, Na_2CO_3 and $NaHCO_3$)	Response surface methodology	Flavonoids	Anti-oxidant	D	[14]
Magnolia officinalis stalk bark	Water	AGO-2 planetary activator (Russia)	Na_2CO_3 .	One-way ANOVA with SNK test for a multiple comparison	Magnolol	n.a.	E	[15]
Phyllostachys edulis Leaves	Alkali solution	AGO-2 planetary ball mill (Novic, Russia) equipped with a water-cooling system	Na_2CO_3 and $Na_2B_4O_7{\cdot}10H_2O$	One-way ANOVA with SNK test for a multiple comparison	Flavonoids	n.a.	F	[16]
Ginkgo biloba leaves	Water	AGO-2 planetary activator	$NaHCO_3$	Response Surface Methodology (RSM) by Box-Behnken Design (BBD)	Flavonoids and terpene trilactones	Anti-oxidant	G	[17]
Hibiscus mutabilis L. Leaves	Water	AGO-2 high intensity planetary mill.	Na_2CO_3 (15.0 wt.%) and $Na_2B_4O_7{\cdot}10H_2O$	One-way ANOVA with SNK test for a multiple comparison	Rutin	n.a.	H	[18]
Ganoderma	Water	AGO-2 high-	NaOH,	Response	Polysacchar	Anti-	I	[19]

lucidum spores		intensity planetary activator using a multimode closed vessel system.	$NaHCO_3$ or Na_2CO_3	Surface Methodology (RSM) by Box-Behnken Design (BBD)	ides	oxidant		
Acanthopanax senticosus	Water	Vibrational mill	Na_2CO_3	n.a.	Isofraxidin	n.a.	J	[20]
Gardenia jasminoides fruit	Water, alcohal	Planetary ball mill (Retsch, Haan, Germany)	Active carbon	n.a.	Gardenia Yellow and Geniposide	n.a.	K	[21]
Raw tea	Water	Ball crusher (QM-WX04, Nanjing DaRan Technology Co. Ltd. Nanjing, China.)	Sodium carbonate and sodium borohydrate	Response Surface Methodology (RSM) by Central composite Design (CCD)	Phenolic content	n.a.	L	[22]

A= Concentration increased up to 10 times with respect to traditional method, environmental friendly and reduce processing time; B= Antioxidant activities of the extracts from planetary activator with water as solvent were higher and stronger than heat reflux method; C= In the specific case of isofraxidin, significant enhancement and shorter time required over heat-reflux and superfine grinding extraction was observed; D= It is highly effective for poorly water-soluble components; E= High yield of magnolol due to disruption of cell walls, better extraction selectivity, ecofriendly, less extraction time and lower extraction temperature, simplification of sample preparation and highly effect for water insoluble components; F= Eliminate diffusion hindrances, chemical transformations promote the progression of the subsequent extraction, fast and effective at room temperature and preventing leaching of excessive chlorophyll into extraction solvent; G= Mechanochemical extraction have notable advantages of reducing organic solvent, saving time, low temperature and higher efficiency; H= During the Mechanochemical process, both the higher diffusivity and the enhanced water solubility of the target compound(s) could significantly increase the speed of extraction. The main advantages of MCAE approach are enhanced extraction efficiency, no organic solvent consumption and much lower extraction temperature. and highly effect for water insoluble components; I= Reduction in total extraction time was shorter and the extraction temperature was lower; J= Mechanochemical extraction employed low temperature and shorter extraction time which helped in minimizing the cost and improving the extracting efficiency; K= Low consumption of both energy and solvent ; L= Water can be used as leaching reagent for tea polyphenols leaching process at room temperature with the application of Mechanochemical methodology.

Method of Sample Preparation:

Water is used as common solvents in all method of preparation. Sodium carbonate is used as common solid reagent. The entire sample was centrifuged and acidified using different solvents such as acetic acid, citric acid. List of method of preparation of sample was mentioned in table 2.

Table 2: List of Method of Sample preparation using Mechanochemical assisted Extraction

List of plants	Methodology of Sample Preparation	Reference
Salvia Miltiorrhiza Bunge	Plant material was oven-dried, sliced and crushed. Samples were mixed with different concentrations of aqueous Ionic liquid solutions and then processed in the ball mill. The suspension was centrifuged, and collected for analysis	[11]
Camellia oleifera Abel. Meal	Defatted powder and different amounts of solid reagent were added into a planetary activator, extracted with water, centrifugation at 4700 rpm for 15 min. The supernatant was acidified to pH5.0 with acetic acid and evaporated in a vacuum of 0.09 MPa at 55 °C for 40 min.	[12]
Eleutherococcus senticosus roots and rhizome	Prepared sample was mixed with the solid content Na_2CO_3 and appropriate volume of solvent. Supernatants were acidified to pH 4.0 and evaporated by a rotary evaporator under vacuum at 40 °C. Residues were rinsed twice with 5 mL of water	[13]
Sophora flavescens Root	*S. flavescens* roots, solid reagents, and stainless steel balls were added into a vial (PM-200 planetary mill, Retsch, Haan, Germany). After co-grinding at 400 rpm for 10 min, the powders were extracted with water for 20 min and then centrifuged at 3077 g for 10 min. The solution pH was adjusted to 4–5 with citric acid. The solution was condensed, centrifuged at 9391 g, the supernatant was discarded and the precipitants were analyzed	[14]
Magnolia officinalis stalk bark	Pretreated magnolia stalk bark was ground in AGO-2 planetary activator with a solid basic agent to obtain mechano mixtures. It was then dissolved in water and stirred twice. The supernatant was collected, adjusted to acidic using 6M HCl, and subsequently centrifuged at 2000rpm. The resulting precipitate was freeze-dried to obtain the crude magnolol sample	[15]
Phyllostachys edulis Leaves	Sample and solid reagents were added into AGO-2 planetary ball mill (Novic, Russia). The mixture was ground at 600 rpm for several minutes to obtain a fine powder. It was then extracted and centrifuged at 2000 rpm for 5 min. The supernatant was adjusted to pH 7.0 with 6 M HCl. The liquid product was concentrated under reduced pressure and subsequently made up to a volume of 25 mL with distilled water. The resulting extract was diluted 10 times with distilled water and filtered.	[16]
Ginkgo	Ginkgo leaves (GBE) and solid reagent was added into AGO-2 high-intensity	[17]

biloba leaves	planetary activator. After co-grinding for several minutes, the powder was dissolved in water for a short time. Then the mixtures were centrifuged (4700 rpm, 10 min). The solution pH was adjusted to 5 with dilute acetic acid, then the solution was absorbed into a macroporous resin (ADS- 17). The flavonoids and terpene trilactones were eluted with 70% (v/v) ethanol. The GBE product was obtained after the eluant was concentrated and dried, then weighted.	
Hibiscus mutabilis L. Leaves	Sample was ground with Na_2CO_3 and $Na_2B4O_7{\cdot}10H_2O$ in a high intensity planetary mill AGO-2. The mixture was extracted and centrifuged at 2000 rpm for 5 min, and then the supernatant was adjusted to a desired pH value in the range of 2.0–6.0 with 6 M HCl.	[18]
Ganoderma lucidum spores	Sample was mixed with solid reagent (NaOH, $NaHCO_3$ or Na_2CO_3) into extraction vessel. After co-grinding for several minutes (5–30 min), the powder was extracted with an appropriate volume of water with certain temperature (50–90 °C) and time (30–150 min). Then the mixture was clarified by centrifugation at 4200rpm for 10 min. The supernatant was concentrated by rotary evaporator	[19]
Acanthopanax senticosus	Sample was mixed with Na_2CO_3 content. Sample extracts were further clarified by centrifugation at 8000 rpm for 10 min to separate out the fine particulates. Supernatant was collected, acidified to pH 4.5, and evaporated in a rotary evaporator under vacuum at 40 °C. The residue was rinsed twice with 5 ml water and evaporated to dryness, then dissolved in 20 ml 80 vol. % aqueous ethanol, filtrated	[20]
Gardenia jasminoides fruit	Sample was mixed with active carbon milling at 200 rpm in a planetary mill for 5 min. The extraction conditions of the milled mixtures were extracted with water (liquid-solid Ratio 10:1) at 20 °C for 5 min. 80% ethanol solution (liquid-solid ratio 5:1) and Tween 20 at 75 °C for 5 min to yield gardenia yellow.	[21]
Raw tea	Sample were mixed with Na_2CO_3 and add into the ball crusher for grinding solid phase chemical reaction. A little amount of sodium borohydride was added to system as protective agent in order to prevent TPs from oxidation. The grinded mixed powder was put into the water as leaching agent at room temperature (25±2˚C), continuous stirred water for a certain time. Polymer flocculant (Polyacylamide) was used in the leached solution, which could clear the leaching solution. Took the clean leaching solution by adding dilute hydrochloric acid solution and controlled terminal pH value of the solution were measured in 6.	[22]

Experimental Design:

Experimental design of all medicinal plants using MCAE was compared with microwave extraction (MWE) to compare the extraction time and temperature. The selection of microwave extraction was due to faster extraction method and novel technology. Extraction time for *Camellia oleifera* Abel. after microwave extraction was 35 minutes at 76 °C which is far less as compared to MCAE but temperature is very high which may cause thermal degradation [23]. The optimum extraction time for *Ginkgo biloba* leaves after microwave extraction was 16 minutes which is higher as compared to milting time of MCAE [24]. Although microwave extraction was much effective in *Ganoderma lucidum* spores because of less time at same temperature but it involve the use of ethanol (75%) whereas MCAE are eco-friendly using water as a solvent [25]. Figure 3 represent list of experimental design using MCAE. List of Mechanochemical synthesis/modification of plant based bioactive compounds were mentioned in table 4.

Table 3: List of Experimental design using mechanochemical assisted extraction

List of Medicinal plants	Variable	Range	Optimized Results	Reference
Salvia Miltiorrhiza Bunge	Concentration (mol/L)	0.40-0.60	0.50	[11]
	Solid liquid ratio (g/mL)	0.03-0.07	0.05	
	Time (s)	40.00-80.00	60	
Camellia oleifera Abel. Meal	Ratio of material to solid reagent (g/g)	10:1-30:1	20:1	[12]
	Milling time (min)	5-25	15	
	Extraction time (min)	30-90	60	
	Ratio of solution to solid (mL/g)	15:1-35:1	20:1	
Ginkgo biloba leaves	Amount of solid reagent (%)	10-30	21	[17]
	Ratio of solution to solid (mL/g)	20:1-40:1	33	
	Milling time (min)	3-9	7.5	
Ganoderma lucidum spores	Material ⁄ solid reagent ratio (g/g)	1–15	5	[19]
	Milling time (min)	5–30	20	
	Solution ⁄material ratio (mL/g)	10–30	20	
	Extraction time (min)	30–150	130	
Raw tea	Sodium carbonate content (%)	10-30	25~ 27	[22]
	Solid Material particle size (μm)	30-70	40~ 45	
	Liquid solid mass ratio	40-80	55~ 60	
	Leaving time (min)	5-25	16~18	

Table 4: Mechanochemical synthesis/modification of plant based bioactive compounds

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Instrumentation	Bioactive compounds Synthesis/Modification	Reference
Vibratory mill SPEX-8000 (CertiPrep Inc., USA)	Lappaconitine and Piroxicam	[26]
Not available	Curcumin-Templated Azoles	[27]


Pilot-scale ball mill and Laboratory scale ball mill [28] [11]

FRITSCH Planetary Mill PULVERISETTE 5 classic line (Image courtesy of FRITSCH GMBH) [29]

Conclusion and Future work:

There is lots of advancement in novel extraction methods and instrumentation that leads to greener and environmental friendly atmosphere. Microwave extraction and Ultrasonic assisted extraction were common among them. Mechanochemical assisted extraction is one of an alternative method of extraction. It was fast, efficient way to extract bioactive compounds. Although it is selective method of extraction but researchers are still trying to improve the extraction method on other medicinal plants. Moreover improving the yield by modification of this technique and optimizing the methods that already been used.

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