Application of Novel Drug Delivery System in Enhancing the Therapeutic Potential of Phytoconstituents

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Abstract

Various phytoconstituents obtained from nature have wide biological activities in chronic diseases and have wide therapeutic efficacy. The main advantage of using phytoconstituents is it provides free from adverse effects treatment where none of the medication can do. However, the physiochemical properties such as poor solubility, poor permeation, and non-targeting at the active site will create a barrier which hinders its therapeutic efficacy. So, various nanoformulation strategies are employed to overcome these barriers and provide uniform drug targeting at the active site in desired concentration and improved therapeutic efficacy. These strategies will constitute novel drug delivery systems (NDDS), such as nanoparticles, emulsion-based formulations, liposomes, phytosomes, microspheres, and topical based formulations, are available in commercial level to enhance the bioavailability of the poorly soluble herbal drug. In this review, we highlighted some novel applications of NDDS based approaches for enhancing the therapeutic potential of phytoconstituents having wide biological activities.

Key words: Nanoparticles, novel drug delivery system, phytoconstituents, phytosomes

INTRODUCTION

In modern drug discovery era, various chemically synthesized new molecules are approved by FDA and are coming on the market, having wide therapeutic efficacy, but the adverse effects are associated with this therapy causes serious adverse effects which could be life threatening. Conventional therapy provides non-targetability in tissues and organs due to peak and valley fluctuations, and a frequent dose of administration can produce troublesome for allopathic medicines lead to poor patient compliance.[1] The controlled release drug delivery system provides drug release at a controlled rate and maintains the overall therapeutic concentration of the drug in the body. In ancient times, herbal remedies and natural extract are consumed by people to cure various diseases. These herbal remedies contain hundreds of phytoconstituents present, which is working simultaneously against the disease. In recent times, the interest of people in phytopharmaceuticals has been increasing day-by-day among physicians and patients, and it is evident from the global market of herbal medicine and phytopharmaceuticals that has increased from $18 billion from 2005 and $26 from 2011.[2-4] Various dietary products and supplements are also derived from the natural origin are also gaining more interest in the industry and the global market for phytopharmaceuticals. Some phytoconstituents derived from the natural origin are having a poor solubility and low bioavailability resulting in a narrow therapeutic index, which hinders his novel efficiency, so formulation scientist is working on targeting and controlled drug release of phytoconstituents to provide better therapeutic effect and increased patient compliance.[5,6]

The three main goals of novel drug delivery system (NDDS) is by providing sustained drug release, selected targeting to the site of action and increased patient compliance [Figure 1]. NDDS not only reduce the frequency of administration but also reduce the Peak and valley fluctuations which lead to enhanced bioavailability. The applications of NDDS in phytopharmaceuticals have been widely investigated, and various commercial formulations of phytoconstituents are available in the global market which people will consume...
and take benefit from it. In Phytoformulation research, various drug delivery vehicles, such as liposomes, polymeric nanoparticles, microemulsion, microspheres, solid lipid nanoparticles (SLNs), are used in which phytoconstituent is solubilized and release the drug in a sustained manner.[7-12] The list of drug delivery vehicles used in illustrated in Figure 2. In this review, we highlighted all the important applications of all the nanocarriers for controlled drug delivery of phytoconstituents [Table 1].

**LIPOSOMES**

Liposomes are discovered in 1970 as drug delivery vehicles for targeting at the active site into desired concentration. These are concentric bilayer vesicles in which the aqueous volume is entirely closed by lipid bilayer mainly composed of phospholipids [Figure 3]. Liposomes are biocompatible, non-toxic, and biodegradable in nature; hence, it is widely used in enhancing the therapeutic efficacy of various phytoconstituents. The advantages of liposomes in herbal formulations are given below.[13-15]

- Provides herbal drug release in a sustained fashion
- Reducing peak-valley fluctuations
- Targeting of herbal drug into the desired area
- Improving the solubility and bioavailability of hydrophobic drugs.

There are various methods to prepare liposome-like thin film hydration method, mechanical dispersion method, and rotary film evaporation method. The method is selected based on various factors such as drug loading capacity, the nature of drug, commercial, or lab scale.[14,15] The applications of liposomes in herbal formulations have been investigated widely and its evident from latest researches that are more focused on enhancing the bioavailability of phytoconstituents.[13,16] The potential applications of liposomes in phytoconstituents are given in Table 2.

**POLYMERIC NANOPARTICLES**

The versatility in nanotechnology provides an emerging drug delivery system for targeting the drugs at the desired

<table>
<thead>
<tr>
<th>Table 1: Advantages and disadvantages of CRDDS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
</tr>
<tr>
<td>Eliminates peak-valley fluctuations</td>
</tr>
<tr>
<td>Reduction in dosing frequency leads to poor patient compliance</td>
</tr>
<tr>
<td>Reduction in GI irritation and other dose-related side effects</td>
</tr>
<tr>
<td>Provides sustained release for longer period of time</td>
</tr>
<tr>
<td>Avoidance of night time dosing</td>
</tr>
</tbody>
</table>

GI: Gastrointestinal
Nanoparticles are colloidal particles having submicron size ranges from 10 to 1000 nm. Nanospheres contain a matrix structure in which active pharmaceutical ingredient is entrapped. Nanocapsules contain a membrane made up from polymers in which the API is present in the core of the polymer. Nanoparticles are effective systems for encapsulating a wide variety of drugs from small molecular weight compounds to larger molecules. In recent times, nanoparticles are more focused on herbal drug formulations. The drug release from nanoparticles is either by bulk erosion in the matrix or by surface erosion in the polymer depend on the nature of drug and method of preparation adopted [Figure 4].

There are various methods used for the preparation of nanoparticles, including salting out method, solvent

<table>
<thead>
<tr>
<th>Phytoconstituent</th>
<th>Chemical nature and source</th>
<th>Pharmacological activity</th>
<th>Method of delivering</th>
<th>Clinical significance</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camptothecin</td>
<td>Quinoline alkaloid, obtained from <em>Camptotheca acuminate</em></td>
<td>Useful in ovarian, bladder, colon, and lung cancer</td>
<td>Multilamellar vesicles given orally</td>
<td>Reduction in adverse effects due to improved targeting</td>
<td>17</td>
</tr>
<tr>
<td>Quercetin</td>
<td>Pentahydroxyflavone, obtained from <em>Sophora japonica</em> L.</td>
<td>Antioxidant and antineoplastic</td>
<td>Elastic liposomes</td>
<td>Encapsulation efficiency was increased by 97%</td>
<td>18</td>
</tr>
<tr>
<td>Curcumin</td>
<td>Diarylethylbenzenoid, obtained from <em>Curcuma longa</em></td>
<td>Anticancer, anti-inflammatory, wound healing properties</td>
<td>Transdermal delivery of liposomes</td>
<td>Improved bioavailability and clinical efficacy</td>
<td>19</td>
</tr>
<tr>
<td>Vincristine</td>
<td>Bisindole alkaloid, obtained from <em>Catharanthus roseus</em></td>
<td>Broad spectrum antitumor activity against lung and prostate cancer</td>
<td>Intravenous liposome delivery</td>
<td>Overcome Neurotoxicity problems and other side effects</td>
<td>20</td>
</tr>
<tr>
<td>Catechins</td>
<td>Polyphenolic compounds, obtained from <em>Camellia sinensis</em></td>
<td>Antioxidant, antiobesity, anti-inflammatory, anti-diabetic</td>
<td>Transdermal liposomes</td>
<td>Enhanced bioavailability five-fold higher</td>
<td>21</td>
</tr>
<tr>
<td>Silymarin</td>
<td>Flavonoid, obtained from milk thistle plant <em>Silymarin marianum</em></td>
<td>Hepatoprotective</td>
<td>Buccal liposomal delivery</td>
<td>Enhanced bioavailability and clinical efficacy 2-fold higher</td>
<td>22,23</td>
</tr>
<tr>
<td>Breviscapine</td>
<td>Biphosphonate compound, obtained from <em>Scutellaria barbata</em></td>
<td>Antitumor activity against ovary and breast cancer cells</td>
<td>Injectable multilamellar liposomes</td>
<td>Improved systemic circulation and MRT</td>
<td>24</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Taxol nucleus, obtained from <em>Taxus brevifolia</em></td>
<td>Broad anticancer activity against almost all types of cancer</td>
<td>Injectable liposomal delivery</td>
<td>Improved antitumor activity by selective targeting in cancerous cells</td>
<td>25</td>
</tr>
<tr>
<td>Colchicine</td>
<td>Benzofuran compound, obtained from <em>Colchicum autumnale</em></td>
<td>Anti-gout</td>
<td>Delivering liposome through film dispersion</td>
<td>Optimum encapsulation efficiency and stability</td>
<td>26</td>
</tr>
<tr>
<td>Ampelopsin</td>
<td>Dihydromyricetin, a flavonoid obtained from <em>Cercidiphyllum japonicum</em></td>
<td>Antipyretic, useful in liver disorders</td>
<td>Oral delivery by film ultrasound method</td>
<td>Entrapment ratio is higher, and leakage rate is low in liposomal formulations</td>
<td>27</td>
</tr>
</tbody>
</table>

MRT: Mean residence time

Figure 4: Mechanism of drug release (a) Bulk erosion (b) Surface erosion (Reproduced from ref.30)
Evaporation method, nanoprecipitation, and dialysis method, are widely used for lab scale as well as commercial purposes.\[^{31,32}\] The applications of polymeric nanoparticles in herbal technology have a wide scope and are widely focused.\[^{33-35}\] Studies show clinical significance upon incorporation of herbal drugs into nanoparticles are explained in Table 3.

**EMULSION BASED FORMULATIONS**

Emulsions are thermodynamically unstable formulations of oil and water phase, stabilized by a suitable emulsifying agent. Microemulsions are thermodynamically stable and are isotropic mixtures of oil, water, and surfactant with a droplet size of 100-200 nm (Figure 5). Microemulsion is widely used drug delivery formulations to improve the solubility of poorly soluble drugs. Microemulsions possess various advantages such as good thermodynamic stability, ease of manufacturing, fewer chances of drug degradation, and improved stability.\[^{46,47}\]

The scope of microemulsions in herbal drug delivery is wide and has used clinically as well as commercially.\[^{49,50}\] Curcumin has a wide biological activity like anti-inflammatory, anticancer but have no use clinically because of his poor solubility (1.0 ug/ml) and poor bioavailability (10%), the microemulsion formulation of curcumin has better stability, enhanced drug release up to 97%, and enhanced Cmax leads to enhanced biological activity.\[^{51}\] Studies reporting enhanced bioavailability upon incorporation into microemulsion are given in Table 4.

**PHYTOSOMES**

The term phytosome is derived from two words, “Phyto” means plant and Some” means cell. Phytosome is a patented technology developed by a leading industrialist in phytopharmaceuticals to produce lipid drug molecular

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**Table 3: Studies reporting enhanced bioavailability after incorporation into polymeric nanoparticles**

<table>
<thead>
<tr>
<th>Phytoconstituent</th>
<th>Chemical nature and source</th>
<th>Pharmacological activity</th>
<th>Clinical significance upon incorporation</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypericin</td>
<td>Naphthodianthrone, obtained from <em>Hypericum perforatum</em></td>
<td>Photosensitizer used in radiotherapy</td>
<td>Improved lipophilicity in physiologically active media and improved their diagnostic applications</td>
<td>36</td>
</tr>
<tr>
<td>Triptolide</td>
<td>Diterpenoid triepoxide, obtained from Chinese herb, <em>Tripterygium wilfordii</em></td>
<td>Useful in autoimmune disorders, antineoplastic</td>
<td>Improved aqueous solubility and reduced toxic effects due to enhanced targeting into the desired area</td>
<td>37</td>
</tr>
<tr>
<td>Berberine</td>
<td>Isoquinoline compound, obtained from <em>Berberis aquifolium</em></td>
<td>Anticancer</td>
<td>Sustain the delivery of phytoconstituent lead to enhanced duration of action</td>
<td>38,39</td>
</tr>
<tr>
<td>Ginseng</td>
<td>Steroidal compound, obtained from <em>Panax ginseng, Panax quinquefolius</em></td>
<td>Antioxidant activity</td>
<td>Enhanced stability, therapeutic action, and drug release</td>
<td>40</td>
</tr>
<tr>
<td>Tertandrine</td>
<td>Bis-isoquinoline alkaloid, obtained from <em>Stephania tetrandra</em></td>
<td>Calcium channel blocker</td>
<td>Improved vasodilatory activity</td>
<td>41,42</td>
</tr>
<tr>
<td>Naringenin</td>
<td>Coumarin compound, obtained from <em>Glycyrrhiza glabra</em></td>
<td>Immunomodulator</td>
<td>Improved drug loading and antioxidant activity</td>
<td>43,44</td>
</tr>
<tr>
<td>Glycyrrhizic acid</td>
<td>Steroidal saponin, obtained from <em>Glycyrrhiza glabra</em></td>
<td>Antihypertensive, useful in hepatitis</td>
<td>Improved drug release and encapsulation efficiency</td>
<td>45</td>
</tr>
</tbody>
</table>

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**Figure 5: Illustration of differences in the size range between micro and nanoemulsion (Reproduced from Ref. 48)**
complexes. Phytosome contains herbal drug or phytoconstituent entrapped in an aqueous core surrounded by a lipid bilayer, consists of phosphotidylcholine. The phosphotidylcholine moiety has gastroprotective properties, protect the drug from the degradation by gastric enzymes and secretions. While comparing with a liposome, which is the composition of water-soluble substance with phospholipid in a definite proportion with no chemical bonds formed, the phytosome contain herbal drug with phosphotidylcholine in a different ratio depending on the molecule complexed with the formation of chemical bonds. Phytosome found superior to liposome in topical delivery and skin permeation enhancement. Phytosome has improved pharmacokinetic and pharmacodynamics parameter that used to enhance the bioavailability of many popular herbal extracts including milk thistle, grape seed, and gingko biloba. Phytosome is more bioavailable and enhanced solubilization capacity to cross the lipid bilayer membrane and then reaches the systemic circulation and provides therapeutic effect.  

Phytosome has wide research in phytoconstituents of biological origin, and few commercial products are available in the market [Figure 6] which the people take profit of it. Table 5 describes studies which enhance the bioavailability of phytoconstituents upon incorporation into phytosomes.  

**MICROSPHERES**

Microspheres are solid, almost spherical in nature, having a diameter in the range of 1 um-1000 um in which drug is dispersed in finely divided form or crystalline form. Microspheres are made up of various polymeric materials including natural polymers such as albumin, gelatin, and chitosan; or synthetic polymers including polylactic acid...
and polyglycolic acid and waxes such as beeswax and carnauba wax. Microspheres are having wide commercial applications including sustained drug delivery, overcome handling issues with potent molecules and improved targeting at the active site in desired concentration to maintain overall effective plasma concentration for a longer period of time.[74,75]

The release mechanism of microsphere follows first order kinetics having dissolution and diffusion are two main mechanisms for drug release. The outer layer of polymer is first dissolved, and the dissolution media will diffuse the polymer matrix makes the entrapped drug to release in the matrix. The rate of drug release depends on the type of matrix used and drug/polymer concentration.[76]

Microspheres are widely used as drug delivery carrier for targeting of various agents that cause dose-dependent adverse effects. In recent times, microspheres are widely used to enhance the therapeutic potential of various poorly soluble phytoconstituents. Various techniques such as gastroretentive bloating microspheres, microencapsulation, emulsification, and calcium alginate based beads are used widely for herbal drug delivery. Table 6 shows the studies enhancing the therapeutic potential of phytoconstituents upon incorporation into microspheres.

**TOPICAL DRUG DELIVERY APPROACHES**

Delivery of phytoconstituents via skin is widely investigated for enhancing permeation and therapeutic efficacy. The topical delivery possesses major advantages such as avoidance of first pass metabolism, decrease adverse effects associated with oral and intravenous (IV) doses, effective maintenance of cars, and improved therapeutic efficacy. Various strategies are used to enhance the transdermal permeation including transdermal patches, ethosomes, transferosomes, and SLNs.[83-85]

Transdermal patches are the novel approach which utilizes permeation enhancers (Terpenes, ozone, and surfactants) for topical delivery. Various physical methods are used such as iontophoresis, sonophoresis, microneedles, and skin electroporation for delivery of the drug through a transdermal patch. The transdermal patch utilizing rate controlling membrane to sustain the delivery of the drug via the skin into the blood stream.[86,87] The main limitation in transdermal patch approach that it causes skin irritation or skin infection due to the high frequency applied through iontophoresis, which will overcome by the novel vesicular carriers such as transferosomes and ethosomes, which supplies essential nutrients results in maintain the integrity of the skin. Ethosomes are phospholipid based vesicles contains a high
content of ethanol (20-50%) which itself act as a permeation enhancer in transdermal delivery. Compare to other carriers, ethosomes have the capability to permeate the drug more deeply and more efficiently into the systemic circulation.[88,89]

On the other hand, transferosomes are also used as potential carriers for topical delivery. Transferosomes utilizing the osmotic pressure and hydration to increase permeation. These two vesicular carriers are widely used in topical drug delivery.

**Table 6: Studies reporting enhanced bioavailability upon incorporating herbal drug into microspheres**

<table>
<thead>
<tr>
<th>Phytoconstituent/Plant name</th>
<th>Chemical nature and source</th>
<th>Pharmacological activity</th>
<th>Clinical significance</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rutin</td>
<td>Flavonoid glycoside, obtained from <em>Carpobrotus edulis</em></td>
<td>Antioxidant</td>
<td>Microspheres shows sustained release behavior for the drug within 20 h, and still maintain existed within 180 h</td>
<td>77</td>
</tr>
<tr>
<td>Zedoary essential oil</td>
<td>Essential oil, obtained from <em>Curcuma zedoaria Roscoe</em></td>
<td>Hepatoprotective</td>
<td>3-fold higher bioavailability as compare to conventional formulation</td>
<td>78</td>
</tr>
<tr>
<td>Camptothecin</td>
<td>Quinoline alkaloid, obtained from <em>Camptothecin acuminata</em></td>
<td>Antineoplastic</td>
<td>CPT encapsulated in PLGA microspheres should retain its antitumor potency for longer period of time</td>
<td>79</td>
</tr>
<tr>
<td>Quercetin</td>
<td>Pentahydroxyflavone, obtained from <em>Sophora japonica</em> L.</td>
<td>Antioxidant and anti-inflammatory</td>
<td>Controlled drug delivery for effective management of arthritis</td>
<td>80</td>
</tr>
<tr>
<td>Ginsenosides</td>
<td>Steroidal glycoside, obtained from <em>Panax</em> species (<em>Panax ginseng, Panax notofolium</em>)</td>
<td>Anticancer, Immunomodulator</td>
<td>PLA microspheres shows improved drug release behavior and encapsulation efficiency</td>
<td>81</td>
</tr>
<tr>
<td>Silymarin</td>
<td>Flavolignan, obtained from milk thistle plant (<em>Silybum marinus</em>)</td>
<td>Hepatoprotective</td>
<td>Floating microspheres of silymarin exhibited prolonged drug release and excellent stability</td>
<td>82</td>
</tr>
</tbody>
</table>

CPT: Camptothecin, PLGA: Poly (D, L-Lactic-co-Glycolic Acid), PLA: Polylactide

**Table 7: Studies reporting enhanced permeation and therapeutic efficacy upon incorporating herbal drug into various topical delivery strategies**

<table>
<thead>
<tr>
<th>Phytoconstituent/plant</th>
<th>Pharmacological activity</th>
<th>Formulation strategy</th>
<th>Clinical significance</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Khellin</td>
<td>Anti-acne, used in psoriasis</td>
<td>Transdermal patch using iontophoresis</td>
<td>Transdermal gel containing khellin was able to permeate more deeply and provide more effective treatment of psoriasis</td>
<td>93</td>
</tr>
<tr>
<td>Caffeine from the extract of <em>Paulinia cupana</em></td>
<td>CNS stimulant</td>
<td>Transdermal patch</td>
<td>Transdermal patch was effective releasing all components simultaneously as compare to commercial formulation</td>
<td>94</td>
</tr>
<tr>
<td>Sophora alopecuroides</td>
<td>Anticancer and anti-inflammatory</td>
<td>Ethosomes</td>
<td>Ethosomes containing drug bypass the first pass metabolism and reaches drug more deeply into the skin for therapeutic effect</td>
<td>95</td>
</tr>
<tr>
<td>Matrine</td>
<td>Antibacterial</td>
<td>Ethosomes</td>
<td>Ethosomes containing matrine enhances the permeation and antibacterial effect</td>
<td>96</td>
</tr>
<tr>
<td>Curcumin</td>
<td>Anticancer, antioxidant and anti inflammatory</td>
<td>Transfersomes</td>
<td>Formulation shows higher entrapment efficiency and higher permeation of drug from transfersomal gel</td>
<td>97</td>
</tr>
<tr>
<td>Capsaicin</td>
<td>Analgesic and anti-rheumatic</td>
<td>Transfersomes</td>
<td>Better analgesic activity via topical delivery as compare to commercially available oral formulation</td>
<td>98</td>
</tr>
<tr>
<td>Vincristine</td>
<td>Antimitotic</td>
<td>Transfersomes</td>
<td>Compare to oral and IV formulation, the retention time of topical formulation in extended by 12 h</td>
<td>99</td>
</tr>
<tr>
<td>Triptolide</td>
<td>Used in auto-immune disease</td>
<td>SLNs</td>
<td>The anti-inflammatory activity is higher in SLN dispersion for rheumatoid arthritis</td>
<td>100,101</td>
</tr>
</tbody>
</table>

CNS: Central nervous system, IV: Intravenous, SLN: Solid lipid nanoparticles
delivery to enhance the permeation and therapeutic efficacy of phytoconstituents.\[90\]

SLNs are widely used drug delivery carriers for topical application. SLN comprises lipid excipients which become solid at room temperature. SLN has a mean diameter of colloidal nature ranges from 50-1000nm. The advantages of SLNs, including potential targeting at the active site in desired concentration, prevent degradation of drugs, improved drug loading and encapsulation efficiency, and reduction of drug toxicity. Various methods are used for the preparation of SLNs including homogenization, microemulsion, ultrasonification, and solvent diffusion method.\[91,92\] These topical approaches would prove as an effective drug delivery of phytoconstituents as compared to oral and IV. Table 7 shows various studies which increase permeation of phytoconstituents through topical drug delivery strategies.

### CONTROLLED RELEASE DEVICES

Various approaches are used to enhance the therapeutic efficacy of phytoconstituents by formulating into controlled release drug delivery system. The versatility of this system

<p>| Table 8: Recent patients on novel drug delivery system of phytoconstituents |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|</p>
<table>
<thead>
<tr>
<th>Patient number</th>
<th>Inventor</th>
<th>Publishing date</th>
<th>Description</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>US 20140141108 A1</td>
<td>Kenneth Brown, Brandi M Scott</td>
<td>2014-05-22</td>
<td>This present invention relates to an herbal composition (red quebracho extract) that treats various diseases, including bloating, constipation and there of</td>
<td>107</td>
</tr>
<tr>
<td>US 20070042062 A1</td>
<td>Palpu Pushpangadan, Chandana Rao, Ajay Rawat, Dadala Kumar</td>
<td>2007-02-27</td>
<td>This present invention relates to novel herbal formulation contain Curcuma longa and Zingiber officinale Linn. rhizomes extract for the treatment of diabetes mellitus</td>
<td>108</td>
</tr>
<tr>
<td>US 7968115 B2</td>
<td>Razelle Kurzrock, Lan Li, Kapil Mehta, Bharat Bhushan Agarawal</td>
<td>2011-06-28</td>
<td>This present invention relates to the novel liposomal formulation of curcumin for the treatment of pancreatic, breast, and melanoma cancer</td>
<td>109</td>
</tr>
<tr>
<td>US 6312736 B1</td>
<td>Gregory J. Kelly, Ann Perry</td>
<td>2001-11-06</td>
<td>This present investigation deals with various extracts such as white willow bark extract, kava kava root extract, feverfew extract, ginger root extract, Guarana extract for the relief of pain and its associated conditions</td>
<td>110</td>
</tr>
<tr>
<td>US 20100104646 A1</td>
<td>Ji Hwal Kim</td>
<td>2010-04-29</td>
<td>This present invention deals with nanoparticle composition comprises mixture of Zanthoxylum pipentum, Cnidium officinale encapsulated It using lecithin and chitosan to produce lecithin-capsuled nanoparticles</td>
<td>111</td>
</tr>
<tr>
<td>EP 2437725 A1</td>
<td>Manu Chaudhary, Vijay Naithani</td>
<td>2012-04-11</td>
<td>This present invention deals with topical microemulsion composition comprises various ratio of oil, water, and surfactant and herbal phytoconstituent includes Piper nigrum, Zingiber officinale, Piper longum, Cinnamomum zeylanicum, Cinnamomum tamala, Vitex negundo, Boswellia serrate that will used for the treatment of rheumatoid arthritis</td>
<td>112</td>
</tr>
<tr>
<td>US 6703034 B2</td>
<td>Balraj S. Parmar, Manoj Varshney, Dinesh O. Shah</td>
<td>2004-03-09</td>
<td>This present invention deals with the microemulsion composition of neem oil contain oil, non-ionic surfactant, and water for the treatment of various diseases</td>
<td>113</td>
</tr>
<tr>
<td>US 20050042271A1</td>
<td>Weihong Xiong, Dinesh Patel</td>
<td>2005-02-24</td>
<td>This present investigation deals with alkaloids of Aconitum species incorporated in a transdermal drug delivery system for the treatment of pain and inflammation</td>
<td>114</td>
</tr>
<tr>
<td>WO 2005034923 A1</td>
<td>Dominique Marechal, Wel-Hong Yang, Yu-Zhang Hu</td>
<td>2005-04-21</td>
<td>This invention deals with the formulation of sustained release granules of gingko biloba extract as well as the process for preparing it</td>
<td>115</td>
</tr>
</tbody>
</table>
is explained by first marketed controlled release product known as ocusert®. Ocusert is a controlled release product used for topical delivery of eye for the treatment of open eye glaucoma. Ocusert contains pilocarpine as an active pharmaceutical ingredient, aparasymptomimetic alkaloid obtained from various species of pilocarpus, mostly from Pilocarpus Jaborandi and Pilocarpus Microphyllus. This device will provide sustained drug delivery for a longer period of time.[102]

Another approach of controlled drug delivery is by formulating into polymeric implants. Implants are polymeric devices which provide controlled drug delivery of wide variety of drugs. However, its scope is wide in enhancing the therapeutic efficacy of phytoconstituents in a sustained manner.[103] Danshen is an active phytoconstituent obtained from Radix Salviae Miltiorrhizae, is formulated into implant contain chitosan and gelatin as a natural polymer enhances the therapeutic efficacy of healing muscles and tissues in the abdominal cavities.[104]

Micropellets are also the widely used controlled release device for sustained drug delivery. It is made up of solid particles in the range of 1-1000 um. Micropellets are widely used for taste masking, enteric coating, and preventing drug degradation from biological environment. It also used for delivery of two incompatible drugs simultaneously at same or different sites.[105] Curcumin were formulated into Pectin-hydroxypropyl methylcellulose coated pellets which provide sustained drug delivery and gives better results for inflammatory disease [Table 8].[106]

REFERENCES

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