

# Phytochemical Screening, GC-MS Analysis and Total Phenolic Content Determination of Bioactive Compound of Propolis

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## ABSTRACT

India is a hub for a large variety of natural products that have proven their therapeutic efficacy in various ailments and disorders. Despite it, a lot of natural products are yet to be explored, and Indian propolis is one of them. Indian propolis is a waxy natural product obtained from beehives. In this research, phytochemical constituents present in Indian propolis were qualitatively analyzed using phytochemical screening, gas chromatography-mass spectroscopy (GC-MS), and quantitatively using total phenolic content. Phytochemical screening results revealed the presence of total phenolic content, saponins, glycosides, alkaloids, terpenoids, proteins, steroids, flavonoids, oils & resins supported by GC-MS results. The GC-MS analysis revealed the presence of 17 different constituents having higher peak areas. Amongst these 17 bioactive compounds, oxirane, phenyl ethyl alcohol, caffeine, chrysene, riboflavin and 2-aminophenol were found to have higher peak areas of 5.78, 4.58, 4.46, 3.11, 2.65 and 2.56%, respectively. The results of total phenolic contents revealed the presence of 23 different constituents in different concentrations amongst ellagic acid, kaempferol, epicatechin, galangin, and quercetin were present in rich amounts 538.73, 402.34, 234.85, 121.95 and 95.3 µg/kg, respectively. These constituents are well known for their therapeutic efficacy, which is an indication for the exploration of the therapeutic efficacy of Indian propolis in the future.

**Keywords:** Indian propolis, Phytochemical screening, Gas chromatography-mass spectroscopy, Total phenolic content.

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## INTRODUCTION

During the last century, tremendous advancements have been achieved in natural source-based drugs. In recent decades, great advances came in notice in modern medicines; plants still contribute to health care. Propolis is a particular natural product from apiculture and is a vital, healthy food element with medicinal and nutritional benefits. Its chemical components have been thoroughly investigated in many parts of the world, and intriguingly, it was discovered that the majority of them contain various phytochemical components. The primary ingredients in various types of raw propolis have been identified as a group of polyphenols, terpenoids, steroids, sugars, and amino acids.<sup>1</sup> Despite such vast research on propolis obtained from different regions globally, the Indian propolis is yet to be explored. The chemical constituents of Indian propolis differ based on different geographical sources and is accessible throughout India.<sup>2</sup> There are various techniques, namely preliminary phytochemical screening, GC-MS analysis, and total phenolic content determination

for qualitative and quantitative analysis of a compound. GC-MS is a sophisticated analytical technique used for further confirmation of the constituents obtained after the preliminary phytochemical screening. Phenolic components comprise most propolis samples, and several polyphenolic chemicals have been discovered as clues to propolis quality in various forms.<sup>3</sup>

## MATERIAL AND METHODS

### Drug Procurement

Indian propolis extract powder sample was purchased and collected from Vital herbs, Uttam Nagar, Delhi GSTIN-07CIRPD7950H1ZV in June 21; the batch number was VH/PE/VHP012. The sample appearance was brown fine powder. Bulk density was 49.2 g/100 mL.

### Preparation of Extracts

The propolis sample (1 g) was suspended in absolute ethanol (10 mL), vortexed and sonicated for 1-hour at room temperature. Under the fume hood, the samples were held in the dark for 12 hours before being centrifuged for 10 minutes at 2000 rpm.

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At room temperature, the supernatants were taken apart and left to dry. The yield of each extract was recorded, and the ethanolic extracts of the Indian propolis samples were kept at a temperature of  $-20^{\circ}\text{C}$  until further usage.

### Preliminary Phytochemical Screening

Phytochemical screenings were performed to check the presence of phytochemical constituents like alkaloids, flavonoids, phenols, terpenoids, and coumarins by performing the standard methods using Dragendorff's test, Shinoda's test, lead acetates test, noller's test, alcoholic NaOH test respectively.<sup>4</sup>

### Gas Chromatography-Mass Spectroscopy (GC-MS)

#### Analysis

A 7890 Agilent Technologies (Auto system) was used to conduct the GC-MS analysis. Gas chromatograph outfitted with mass detector 7000 GC/MS Triple Quad and connected to it, as well as 7693A autosampler outfitted with column HP 5MS 30M. 1-mL/minute of helium was employed as the carrier gas. The oven's temperature was originally maintained at  $36^{\circ}\text{C}$  for 5 minutes before being raised to  $150^{\circ}\text{C}$  at a rate of  $4^{\circ}\text{C}/\text{minute}$ . The temperature was then raised to  $250^{\circ}\text{C}$  after 5 minutes at a rate of  $20^{\circ}\text{C}/\text{minute}$ . By comparing the mass spectra of the compounds to data and literature from the National Institute of Standard and Technology (NIST) library, the compounds were identified based on their retention times.

### Total Phenolic Content (TPC)

The TPC determination was carried out using a liquid chromatography-mass spectrometry (LC-MS) 6470 Agilent Technologies (Auto system). The autosampler has column C18-150 mm, an injection volume of  $5\ \mu\text{L}$ , and a column temperature of  $37^{\circ}\text{C}$ . The column flow was maintained  $0.5\ \text{mL}/\text{minute}$ . The temperature of oven was initially held at  $36^{\circ}\text{C}$  for 5 minutes and increased to  $150^{\circ}\text{C}$  at the rate of  $4^{\circ}\text{C}/\text{min}$ . Finally, the temperature was raised by  $20^{\circ}\text{C}$  every minute for 5 minutes, bringing it to  $250^{\circ}\text{C}$ .

## RESULTS AND DISCUSSION

### Preliminary Phytochemical Screening

The presence of different phytochemical constituents in ethanolic extracts of Indian propolis was evaluated qualitatively, as mentioned in Table 1.

Phytochemical analysis of an ethanolic extract of the Indian propolis showed the presence of alkaloids, flavonoids, glycosides, anthraquinones, saponins, terpenoids, phlobatannin, tannins, volatile oil, steroids, proteins, amino acids, quinones, phenols, coumarins and fixed oil which have proven their efficacy as anticancer, neuroprotective, antifungal, anti-inflammatory, hepatoprotective activities and antioxidant activities.<sup>4</sup>

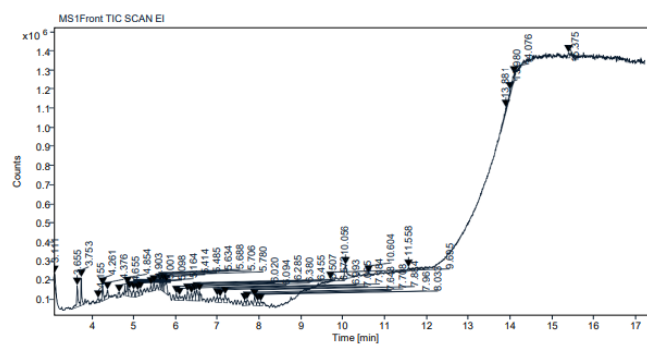
### Gas Chromatography-Mass spectrometry Analysis

The chromatogram obtained on GC-MS analysis has been depicted in Figure 1. The chromatogram was interpreted using the obtained values of retention time, peak area, Chemical

**Table 1:** Preliminary phytochemical evaluation of ethanolic extract of Indian propolis

Phytochemical constituents	Reagents	Result
Alkaloids	Dragendorff's test	+
Anthraquinones	Borntrager's test	+
Glycosides	Anthrone + Conc. $\text{H}_2\text{SO}_4$	+
Flavonoids	Shinoda's test	+
Terpenoids	Noller's Test	+
Saponins	Foam test/Frothing test	+
Phlobatannin	1% HCl	+
Quinones	Conc. $\text{H}_2\text{SO}_4$	+
Steroids	Liebermann-Burchardt test	+
Volatile Oil	Strin test	+
Protein/Amino acids	Biuret test Ninhydrin test	+
Tannins	Braemer's test	+
Phenols	Lead acetates test, Phenol Test	+
Coumarins	Alcoholic NaOH	+
Fixed Oil	Spot test	+

+ = Present



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**Table 2:** Different bioactive substances detected in ethanolic extract of Indian propolis along with their documented biological activities

Name of the Compounds	Retention Time (min)	Peak Area%	Molecular Formula	Probability %	Reported Biological Activity
Octasiloxane, 1,1,3,3,5,5,7,7,9,9, 11,11,13,13,15,15-hexadecamethyl	3.11	3.33	C <sub>16</sub> H <sub>48</sub> O <sub>7</sub> Si <sub>8</sub>	62.93	Antimicrobial <sup>5</sup>
Oxirane, [(2- propenyloxy)methyl]	3.653	5.78	C <sub>6</sub> H <sub>10</sub> O <sub>2</sub>	6.33	Antifungal <sup>6</sup>
Phenylethyl Alcohol	3.75	4.58	C <sub>8</sub> H <sub>10</sub> O	21.88	Sedative <sup>7</sup> Antifungal <sup>8</sup>
Orcinol	4.156	1.42	C <sub>7</sub> H <sub>8</sub> O <sub>2</sub>	5.72	Anxiolytic <sup>9</sup> Radical scavenging effect <sup>10,11</sup> Bone formation <sup>12</sup> Antiproliferative <sup>13</sup> Anticancer <sup>14</sup> and Anti-depressant activity <sup>9,15</sup>
2-Hydroxy-3- methoxybenzyl alcohol	4.374	2.89	C <sub>8</sub> H <sub>10</sub> O <sub>3</sub>	6.57	Anti-proliferative <sup>16</sup> And Antiviral activity <sup>17</sup>
Heptasiloxane, 1,1,3,3,5,5,7,7,9,9,11,11, 13,13-tetradecamethyl heptasiloxane	4.654	1.56	C <sub>14</sub> H <sub>42</sub> O <sub>6</sub> Si <sub>7</sub>	6.98	Insecticidal <sup>18</sup> Anticancer, Cytochrome P450 2E1 inhibitor <sup>19</sup>
2-Aminophenol	4.854	2.65	C <sub>6</sub> H <sub>7</sub> NO	4.06	Fungicidal Intermediate for anti-malarial drugs <sup>20</sup>
5H-Cyclopropa-[3,4]benz[1,2- e]azulen-5-one, 9,9abis (acetyloxy)-3-[(acetyloxy)methyl]-1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4,4a,7b-trihydroxy-1,1,6,8-tetramethyl	5.003	2.06	C <sub>26</sub> H <sub>34</sub> O <sub>10</sub> CC <sub>6</sub> H <sub>7</sub> NO	4.14	No reported activity
6,8-Difluoro-2,2,4,4,6,7,7,8,9,9-decamethyl-[1,3,5,2,4,6,7,8,9]trioxahexasilona	5.673	1.96	C <sub>19</sub> H <sub>16</sub> F <sub>3</sub> NO <sub>2</sub>	5.69	No reported activity
Bis[di(trimethylsiloxy)phenylsiloxy] trimethylsiloxyphenylsiloane	5.706	1.69	C <sub>33</sub> H <sub>60</sub> O <sub>7</sub> Si <sub>8</sub>	7.02	Antioxidant <sup>21</sup>
Caffeine	5.78	4.46	C <sub>8</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub>	9.04	Psychostimulant <sup>22</sup> Neuroprotective <sup>23</sup> Alertness <sup>24</sup> Muscle strengthening effect <sup>25</sup> Cognition modulation <sup>26</sup> Wound healing <sup>27</sup> CNS stimulant <sup>28</sup> Antioxidant <sup>29</sup> Anti-inflammatory <sup>30</sup>
Catechins	6.02	1.84	C <sub>15</sub> H <sub>14</sub> O <sub>6</sub>	40.42	Neuroprotective <sup>31</sup> Cardioprotective <sup>32</sup> Anticancer <sup>33</sup> Alzheimer's disease <sup>34</sup> Antidiabetic effect (Type II) <sup>35</sup> Anti-atherosclerotic effect <sup>36</sup> Anti-obesity <sup>37</sup> Anti-viral <sup>38</sup>
Riboflavin	6.283	2.56	C <sub>17</sub> H <sub>20</sub> N <sub>4</sub> O <sub>6</sub>	42.07	Anti-migraine <sup>39</sup> Anti-mycobacterial <sup>40</sup> Crohn's disease <sup>41</sup> Antioxidant <sup>42</sup>
Pantothenic	6.381	2.01	C <sub>9</sub> H <sub>17</sub> NO <sub>5</sub>	64.03	Antioxidant <sup>43,44</sup> Reduces facial acne <sup>45</sup>
Chrysene	6.455	3.11	C <sub>18</sub> H <sub>12</sub>	49.96	Anti-cancer <sup>46</sup> Detoxification <sup>42</sup>
Behenic acid	8.033	1.43	C <sub>22</sub> H <sub>44</sub> O <sub>2</sub>	80.07	Anti-obesity <sup>47</sup> Leishmaniasis treatment <sup>48</sup>

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**Table 3:** The quantitative report of the total phenolic content identified in the ethanolic extract of Indian propolis along with their retention time, response, and concentration

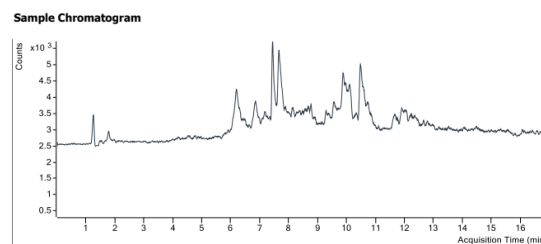
<i>Name of the Compounds</i>	<i>Retention Time (min)</i>	<i>Conc(μg/kg)</i>	<i>Molecular Formula</i>	<i>Reported Biological Activity</i>
Quercetin	1.26	95.3	C <sub>15</sub> H <sub>10</sub> O <sub>7</sub>	Anticancer <sup>49</sup> Neuroprotective <sup>50</sup> Anti-inflammatory, anti-obesity, Antidiabetic (Type II) <sup>51</sup> Hepatoprotective <sup>52</sup> Bacteriostatic <sup>53</sup>
P-Aminobenzoic acid	1.47	15.73	C <sub>7</sub> H <sub>7</sub> NO <sub>2</sub>	Antioxidant <sup>54</sup> Antitubercular <sup>55</sup> Antimicrobial <sup>56</sup>
Ferullic acid	1.5	17.2	C <sub>10</sub> H <sub>10</sub> O <sub>4</sub>	Nephroprotective <sup>57</sup> Antioxidant <sup>58</sup> Anti-inflammatory <sup>59</sup> Anticancer <sup>60</sup> Hypolipidaemic <sup>61</sup>
p-Coumaric acid	1.78	13.52	C <sub>9</sub> H <sub>8</sub> O <sub>3</sub>	Antimelanogenic <sup>62</sup> Antioxidant and antimicrobial <sup>63</sup> Nephroprotective and hepatoprotective <sup>64</sup> Neuroprotective <sup>65</sup> Antidepressants <sup>66</sup>
Naringenin	1.8	0.432	C <sub>15</sub> H <sub>12</sub> O <sub>5</sub>	Hepatoprotective <sup>67</sup> Antiviral and anti-inflammatory <sup>68</sup> Neuroprotective <sup>69</sup> Antidiabetic, cardio-protective and non-glycemic <sup>70</sup> Radioprotective <sup>71</sup>
Syringic acid	1.87	0.456	C <sub>9</sub> H <sub>10</sub> O <sub>5</sub>	Antimicrobial <sup>72</sup> Colorectal Cancer treatment <sup>73</sup> Neuroprotective <sup>74</sup> Antiosteoporotic <sup>75</sup>
Gallic acid	4.87	2.44	C <sub>7</sub> H <sub>6</sub> O <sub>5</sub>	Nephroprotective <sup>76</sup> Anticancer <sup>77</sup> Antidiabetic <sup>51</sup>
Sinapic acid	5.46	17.98	C <sub>11</sub> H <sub>12</sub> O <sub>5</sub>	Anti-ageing <sup>78</sup> Anti-inflammatory <sup>79</sup> Anticancer <sup>80</sup>
Chlorogenic acid	6.22	31.09	C <sub>16</sub> H <sub>18</sub> O <sub>9</sub>	Cognitive enhancement and neuroprotective <sup>81</sup> Hepatoprotective and nephroprotective <sup>82</sup>
Epicatechin	6.85	234.85	C <sub>15</sub> H <sub>14</sub> O <sub>6</sub>	Anticancer, anti-inflammatory, antidiabetic, and neuroprotective <sup>83</sup> Antioxidant <sup>84</sup> Parkinson's disease treatment and neuroprotective <sup>85</sup> Cardioprotective <sup>86</sup>
Hesperidin	7.32	15.34	C <sub>28</sub> H <sub>34</sub> O <sub>15</sub>	Anti-inflammatory <sup>87</sup> Cardioprotective and anticancer <sup>88</sup> Hypotension, anti-inflammatory and antidiabetic effect <sup>89</sup>
Ellagic acid	5.744	538.78	C <sub>14</sub> H <sub>6</sub> O <sub>8</sub>	Antiatherogenic <sup>90</sup> Antioxidative, anti-inflammatory and anti-apoptotic effects, <sup>91</sup> Neuroprotective <sup>92</sup>
Kaempferol	7.45	402.34	C <sub>15</sub> H <sub>10</sub> O <sub>6</sub>	Osteoprotective <sup>93</sup> Anti-inflammatory <sup>94</sup> Anti-obesity and anti-diabetic <sup>95</sup> Antidepressive effect <sup>96</sup> Antifungal <sup>97</sup> Hepatoprotective <sup>98</sup> Anticancer <sup>99</sup>

Caffeic acid	7.5	17.98	C <sub>9</sub> H <sub>8</sub> O <sub>4</sub>	Anti-inflammatory and immunomodulatory <sup>100</sup> Antiproliferative and apoptotic <sup>101</sup> Neuroprotective effect <sup>102</sup>
Chrysin	7.55	0.2	C <sub>15</sub> H <sub>10</sub> O <sub>4</sub>	Antiasthmatic effect, anti-inflammatory, antioxidant and cardioprotective <sup>103</sup> Antidiabetic, Antidyslipidemic and Anti-Inflammatory <sup>104</sup> Antioxidant <sup>105</sup> Antiviral <sup>106</sup>
Apigenin	7.64	98.24	C <sub>15</sub> H <sub>10</sub> O <sub>5</sub>	Neuroprotective <sup>107</sup> Anti-inflammatory <sup>108</sup> Anti-inflammatory <sup>109</sup> Anticancer <sup>110</sup>
Galangin	9.3	121.95	C <sub>15</sub> H <sub>10</sub> O <sub>5</sub>	Antioxidant, cytotoxic, and antigenotoxic <sup>111</sup> Alzheimer's disease <sup>112</sup> Anticancer <sup>113</sup> Metabolic disorder <sup>114</sup>
Coniferaldehyde	9.57	78.75	C <sub>10</sub> H <sub>10</sub> O <sub>3</sub>	Anticancer <sup>115</sup> Cardioprotective <sup>116</sup> Antioxidant activity, antibacterial activity and hypoglycemic <sup>117</sup>
Luteolin	11.01	85.74	C <sub>15</sub> H <sub>10</sub> O <sub>6</sub>	Anti-tumor <sup>118</sup> Periodontitis <sup>119</sup> Anticancer <sup>120</sup> Antidiabetic <sup>121</sup> Nephroprotective <sup>122</sup>
Taxifolin	14.13	0.23	C <sub>15</sub> H <sub>12</sub> O <sub>7</sub>	Antidiabetic <sup>123</sup> Antioxidant, Anti-inflammatory, and Anti-apoptotic <sup>124</sup> Antiallergic <sup>125</sup>
Rutin	16.59	0.46	C <sub>27</sub> H <sub>30</sub> O <sub>16</sub>	Cytotoxic and Apoptogenic <sup>126</sup> Anticancer <sup>127</sup> Hepatoprotective <sup>128</sup>
Pinocembrin	9.3	121.95	C <sub>15</sub> H <sub>12</sub> O <sub>4</sub>	Antioxidant and anti-inflammatory <sup>129</sup> Increasing intestinal motility <sup>130</sup>

documented for antifungal activity. Phenylethyl alcohol has been shown sedative activity. Caffeine has been documented for psychostimulant, neuroprotective, alertness, muscle strengthening, cognition enhancement, wound healing, central nervous system stimulant, antioxidant, neuropsychiatric, anti-inflammatory activities. Chrysenes has shown mainly anticancer activity. Riboflavin has been documented for antimigraine, anti-mycobacterial activities along with treatment of Crohn's disease. 2-aminophenol has been reported for antifungal activity in literature.

### Total Phenolic Content

The chromatogram obtained on TPC analysis has been depicted in the Figure 2. The chromatogram was interpreted using the obtained values of retention time, CAS number, and concentration. Different 23 bioactive compounds were identified: quercetin, p-aminobenzoic acid, ferullic acid, p-coumaric acid, naringenin, ellagic acid, gallic acid, sinapic acid, chlorogenic acid, epicatechin, catechin, hesperidin, syringic acid, kaempferol, caffeic acid, chrysin, cyanidin 3-glucoside, apigenin, syringaldehyde, galangin, pinocembrin,



**Figure 2:** Total Phenolic Content (TPC) Chromatogram of Indian propolis

coniferaldehyde, luteolin, taxifolin, and rutin were identified which has been summarized in the Table 3 along with their documented therapeutic activities from the ethanolic extract of Indian propolis (Figure 2).

Amongst these 23 bioactive compounds, ellagic acid, kaempferol, epicatechin, galangin, and quercetin were present in rich amounts 538.73, 402.34, 234.85, 121.95 and 95.3 µg/kg, respectively. Ellagic acid has been documented for antiatherogenic, antioxidant, anti-inflammatory and antiapoptotic, neuroprotective activity. Kaempferol has been shown to have osteoprotective, anti-inflammatory, anti-obesity,

antidiabetic, antidepressive, antifungal, hepatoprotective, and anticancer activity. Epicatechin has been documented for anticancer, anti-inflammatory, antidiabetic, neuroprotective, antioxidant, Parkinson's disease treatment and neuroprotective, and cardioprotective activity. Galangin has been shown mainly as anti-inflammatory, anticancer, antioxidant, cytotoxic, and antigenotoxic activity. Quercetin has been documented for anticancer, neuroprotective, anti-inflammatory, anti-obesity, antidiabetic (Type II), hepatoprotective, and bacteriostatic activity.

## CONCLUSION

In this study, Indian propolis was found to have various bioactive compounds which have been documented for various pharmacological activities. The GC-MS analysis showed that the presence of 17 and TPC showed the presence of 23 bioactive compounds having numerous pharmacological activities, namely psychostimulant, neuroprotective, muscle strengthening, antioxidant, anticancer, and antidiabetic and cognition enhancement. Various bioactive compounds derived from natural sources have been formulated successfully as nanoformulation like nanoparticles, nanoemulsion, nanosuspension, liposomes, polymeric micelles etc. Hence the bioactive compounds present in Indian propolis can also be formulated as nanoformulation to alleviate various kinds of ailments and diseases using extensive research in this field. It is derived from natural sources owing to few side effects and lower cost, which can benefit society.

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