

## 石榴化学成分及药理活性研究进展

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**摘要** 石榴为石榴科石榴属植物, 其果皮、种子、花、叶、根均可入药, 在我国有着悠久的药用历史。石榴主要化学成分包括鞣质类、黄酮类、萜类、生物碱类、酚酸类、花青素类、脂肪酸类等, 具有抗氧化、降血糖、抗炎、抗肿瘤、抗菌等多种药理作用。本文对石榴各药用部位的化学成分和药理作用进行综述, 以期为其进一步研究和开发利用提供参考。

**关键词** 石榴; 药用部位; 民族药用法; 化学成分; 药理活性

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## Research progress in chemical constituent and pharmacological activity of *Punica granatum* L.

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**Abstract** *Punica granatum* L. (pomegranate) is a medicinal plant belonging to the genus *Punica* Linn. The peel, seed, flower, leaf and root of *P. granatum* is widely used as traditional medicine in China. Phytochemical studies showed that the major chemical constituents of *P. granatum* were tannins, flavonoids, terpenes, alkaloids, phenolic acids, anthocyanins, fatty acids, etc. Biological studies on extracts and active ingredients of *P. granatum* show some bioactivities, such as antioxidant, hypoglycemic, anti-inflammatory, anti-tumor, antibacterial activities. Herein, the chemical constituents and pharmacological effects of different parts of pomegranate were reviewed, providing a theoretical basis for the further research and utilization of pomegranate.

**Key words** *Punica granatum* L.; medicinal part; usage of ethnomedicine; chemical constituent; pharmacological activity

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石榴(*Punica granatum* L.)为石榴科(Punicaceae)落叶灌木或乔木, 又名安石榴, 原产于巴尔干半岛至伊朗及其邻近地区, 汉代传入我国, 江苏、河南等地种植面积较大<sup>[1]</sup>。《中华人民共和国药典》(2020年版)收载石榴皮药材, 具有涩肠止泻, 止血及驱虫等功效<sup>[2]</sup>。本文对近10年国内外学者对于

石榴化学成分及生物活性研究进展进行归纳和概述, 以期为其进一步综合开发利用提供参考依据。

### 1 民族药用法

石榴始载于《名医别录》, 味甘、酸, 无毒, 治下利, 止漏精<sup>[3]</sup>。石榴皮、种子、花、叶、根均可作为药

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用部位,不仅是沿用历史悠久的传统中药,而且在藏族、维吾尔族、苗族等民族均具有广泛的临床应用<sup>[4]</sup>。石榴皮、根、花均被收录于《本草纲目》<sup>[5]</sup>。石榴籽作为藏族习用药材,其味酸、甘,性温,升胃温,助消化,宣肺<sup>[6]</sup>。维吾尔族民族药本草著作《拜地依药书》记载石榴皮、籽、花,二级干寒,味酸涩,止泻止痢、促进创伤愈合<sup>[7]</sup>。苗医学临床应用石榴根治久泻久痢、蛔虫,运用石榴花治疗鼻出血<sup>[8]</sup>。石榴干燥全果是蒙医习用药材之一,主治胃炎,消化不良,腹胀等<sup>[9]</sup>。除此之外,《滇南本草》记载石榴叶敷于患处,可用于治疗跌打损伤<sup>[10]</sup>。

## 2 化学成分

目前,已从石榴各药用部位分离得到多种化合物,主要包括鞣质类、黄酮类、萜类、生物碱类、酚酸类、花青素类、脂肪酸类等。

### 2.1 鞣质类

鞣质是一类结构比较复杂的多元酚类化合物,其结构类型主要包括可水解鞣质和缩合鞣质两大类。鞣质是石榴皮中主要特征性化学成分,而石榴其他药用部位鞣质类成分较石榴皮少<sup>[2,11]</sup>。目前,已从石榴皮、种子、汁、花中发现了30个鞣质类化合物<sup>[12-18]</sup>,包括24个逆没食子鞣质类化合物(1~24),4个缩合鞣质类化合物(27~30)。Ito等<sup>[18]</sup>在石榴假种皮中分离得到了2个新的可水解鞣质低聚体:pomegranins A(25)、pomegranins B(26)。经LC-MS法分析发现,石榴果皮、籽及花中还存在没食子酰葡萄糖苷等没食子鞣质类化合物<sup>[12,14-15]</sup>。具体化合物信息及结构见表1(1~30)、图1。

### 2.2 黄酮类

Derakhshan等<sup>[19]</sup>采用氯化铝比色法测定石榴皮中总黄酮含量约为45 mg/g,远高于籽和汁。石榴皮、种子、汁、花中发现了45个黄酮类化合物<sup>[13-18,20-22]</sup>,包括13个黄酮类化合物(31~43),15个黄酮醇类化合物(44~58),7个二氢黄酮类化合物(59~65),3个异黄酮类化合物(66~68),3个查耳酮类化合物(69~71),4个黄烷醇类化合物(72~75)。具体化合物信息及结构见表2(31~75)和图2。

### 2.3 萜类

石榴种子、汁、花中已发现了10个萜类化合

**Table 1** Tannins in different parts of pomegranate

| No. | Compound                                       | Part <sup>a</sup> | Reference   |
|-----|------------------------------------------------|-------------------|-------------|
| 1   | Sanguisorbic acid dilactone                    | P                 | [12]        |
| 2   | Valoneic acid dilactone                        | P                 | [12]        |
| 3   | Corilagin                                      | S, J, P, F        | [12-14]     |
| 4   | Punicalin                                      | S, J, P           | [12, 15]    |
| 5   | Pedunculagin                                   | P, J              | [12, 15-16] |
| 6   | Terflavin A                                    | P                 | [12]        |
| 7   | Terflavin D                                    | P                 | [12]        |
| 8   | Castalin                                       | P                 | [12]        |
| 9   | Strictinin A                                   | P, J, S           | [17]        |
| 10  | Hippomanin A                                   | P, J, S           | [17]        |
| 11  | Gemin D                                        | P, J, S           | [17]        |
| 12  | Lagerstannin C                                 | P, J              | [17]        |
| 13  | Granatin A                                     | P                 | [12, 15]    |
| 14  | Granatin B                                     | P, J              | [12, 15-16] |
| 15  | Punicalagin                                    | P, J              | [12, 18]    |
| 16  | Tellimagrandin I                               | P                 | [12]        |
| 17  | Casuarinin                                     | P, J              | [12, 17]    |
| 18  | Punigluconin                                   | J                 | [12, 17]    |
| 19  | PedunculaginII                                 | P, J              | [14-15, 17] |
| 20  | Oenothien B                                    | J                 | [18]        |
| 21  | 2-O-Galloylpunicalin                           | P                 | [12]        |
| 22  | Punicacortecin C                               | P                 | [18]        |
| 23  | Eucalbanin B                                   | J                 | [18]        |
| 24  | Eucarpanin T1                                  | J                 | [18]        |
| 25  | Pomegranins A                                  | J                 | [18]        |
| 26  | Pomegranins B                                  | J                 | [18]        |
| 27  | Procyanidin B                                  | P, J, S           | [12-13]     |
| 28  | (+)-Gallocatechin-(4 $\alpha$ →8)-(+)-catechin | P                 | [12]        |
| 29  | (-)-Gallocatechin gallate                      | P                 | [12]        |
| 30  | (-)-Epigallocatechin gallate                   | P                 | [12]        |

<sup>a</sup> The parts include peel (P), seeds (S), juice (J) and flowers(F) of pomegranate

物<sup>[13,18,20-21]</sup>,包括1个裂环烯醚萜苷(76),1个麝子油烷型单环倍半萜(77),2个桉叶烷型双环倍半萜(78,79),2个乌苏烷型五环三萜(80,81),1个羽扇豆烷型五环三萜(82),3个齐墩果烷型五环三萜(83~85)。具体化合物信息及结构见表3(76~85)、图3。

### 2.4 生物碱类

石榴皮中已分离得到了7个生物碱类化合物<sup>[17,23-24]</sup>,主要包括1个单萜类生物碱(86),2个吡咯类生物碱(87,88),4个哌啶类生物碱(89~92)。Li等<sup>[13]</sup>通过LC-MS法从石榴籽中共发现了5个生

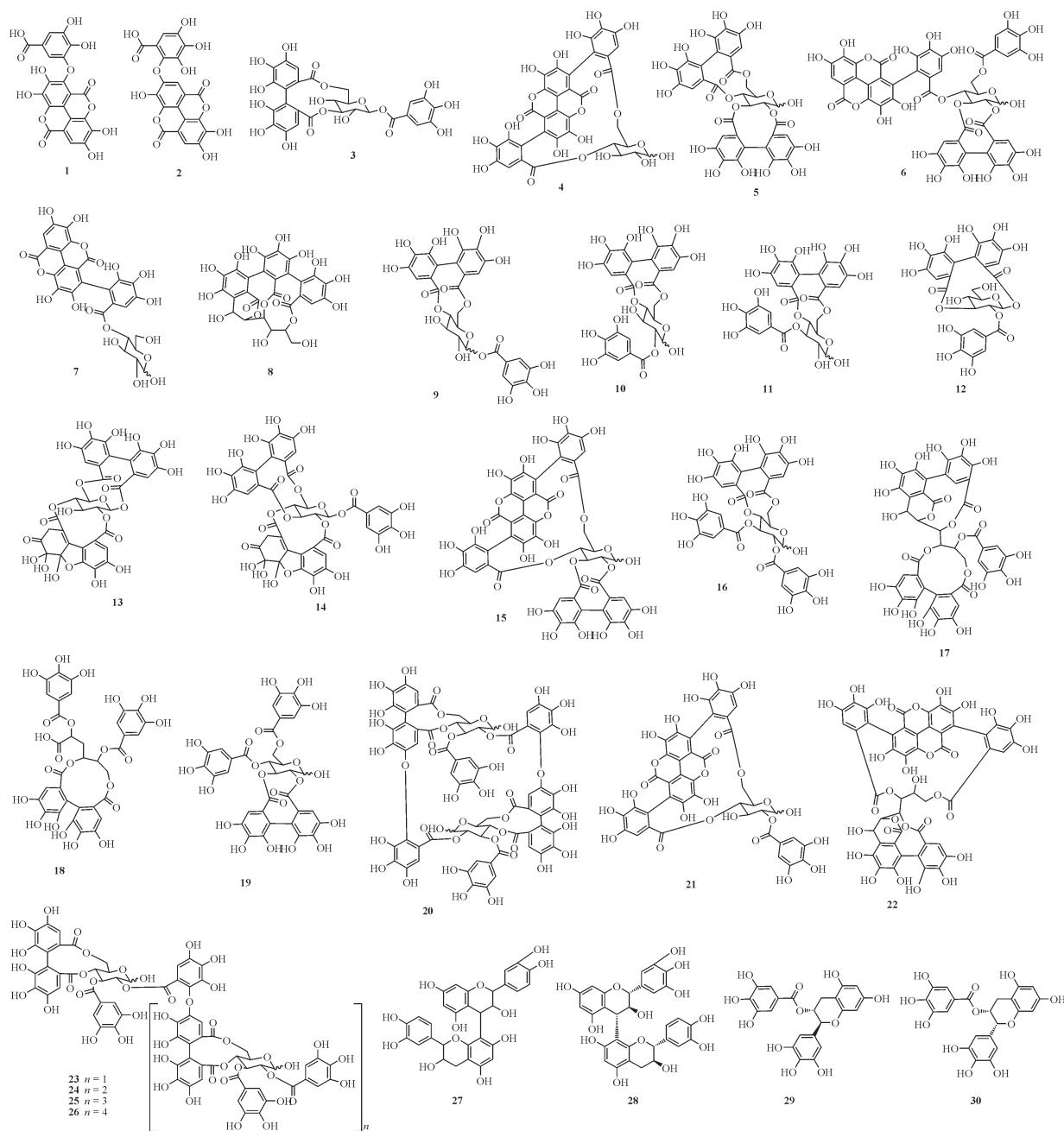


Figure 1 Structures of tannins in different parts of pomegranate

物碱类化合物,包括1个吡啶类生物碱(**93**),2个喹啉类生物碱(**94**, **95**),2个小檗碱类化合物(**96**, **97**)。具体化合物信息及结构见表4(**86** ~ **97**)、图4。

## 2.5 酚酸类

目前,从石榴皮、种子、汁、花中已发现23个酚酸类化合物(**98** ~ **120**)<sup>[12-15,17,20,22]</sup>,主要包括以苯甲酸为母核的C6-C1型化合物、以肉桂酸为母核的C6-C3型化合物及其衍生物。其中,没食子酸(gal-

lic acid)(**115**)和鞣花酸(ellagic acid)(**118**)是石榴皮、籽、花中存在的主要酚酸类化合物<sup>[12-14,19-20]</sup>。具体化合物信息见表5(**98** ~ **120**)。

## 2.6 花青素类

石榴汁、花和皮中富含花青素类成分。目前,已发现了16个花青素类化合物<sup>[14,16,25-27]</sup>,包括2个锦葵色素类(**121**,**122**),1个矮牵牛素类(**123**),3个芍药素类(**124** ~ **126**),4个矢车菊素类(**127** ~ **130**),4个飞燕草素类(**131** ~ **134**),3个天竺葵素类(**135** ~

**Table 2** Flavonoids in different parts of pomegranate

| No. | Compound                                | Structure | Substituent                                                                                 | Part       | Reference        |
|-----|-----------------------------------------|-----------|---------------------------------------------------------------------------------------------|------------|------------------|
| 31  | Luteolin                                | A         | $R_1 = R_2 = R_4 = R_7 = H, R_3 = R_5 = R_6 = OH$                                           | S, J, P, F | [14, 16]         |
| 32  | Luteolin 4'- <i>O</i> -glucoside        | A         | $R_1 = R_2 = R_4 = R_7 = H, R_3 = R_5 = OH, R_6 = O-Glc$                                    | P          | [16]             |
| 33  | Luteolin-3'- <i>O</i> -arabinoside      | A         | $R_1 = R_2 = R_4 = R_7 = H, R_3 = R_6 = OH, R_5 = O-Ara$                                    | P          | [16]             |
| 34  | Cynaroside                              | A         | $R_1 = R_2 = R_4 = R_7 = H, R_3 = O-\beta-D-Glc, R_5 = R_6 = OH$                            | F, S, J    | [14-15]          |
| 35  | Luteolin 3'- <i>O</i> -glucoside        | A         | $R_1 = R_2 = R_4 = R_7 = H, R_3 = R_6 = OH, R_5 = O-Glc$                                    | P          | [16]             |
| 36  | Lonicerin                               | A         | $R_1 = R_2 = R_4 = R_7 = H, R_3 = O-neohesperidose, R_5 = R_6 = OH$                         | S, J       | [14]             |
| 37  | Apigenin                                | A         | $R_1 = R_2 = R_4 = R_5 = R_7 = H, R_3 = R_6 = OH$                                           | S, J, F    | [14-15, 20]      |
| 38  | Cosmosiin                               | A         | $R_1 = R_2 = R_4 = R_5 = R_7 = H, R_3 = O-\beta-D-Glc, R_6 = OH$                            | F, S, J    | [14-15, 20]      |
| 39  | Apigenin-7- <i>O</i> -neohesperidoside  | A         | $R_1 = R_2 = R_4 = R_5 = R_7 = H, R_3 = O-neohesperidose, R_6 = OH$                         | P          | [18]             |
| 40  | Oroxin A                                | A         | $R_1 = R_4 = R_5 = R_6 = R_7 = H, R_2 = OH, R_3 = O-\beta-D-Glc$                            | S, J       | [14]             |
| 41  | Baicalin                                | A         | $R_1 = R_4 = R_5 = R_6 = R_7 = H, R_2 = OH, R_3 = O-D-glucuronide$                          | S, J       | [14]             |
| 42  | Tricetin                                | A         | $R_1 = R_2 = R_4 = H, R_3 = R_5 = R_6 = R_7 = OH$                                           | F          | [15]             |
| 43  | Tricin                                  | A         | $R_1 = R_2 = R_4 = H, R_3 = R_6 = OH, R_5 = R_7 = OCH_3$                                    | F          | [15, 20]         |
| 44  | Morin                                   | A         | $R_1 = R_3 = R_4 = R_6 = OH, R_2 = R_5 = R_7 = H$                                           | S, J       | [14]             |
| 45  | Phellatin                               | A         | $R_1 = R_6 = OH, R_2 = 3-hydroxy-3-methylbutanyl, R_3 = O-\beta-D-Glc, R_4 = R_5 = R_7 = H$ | J          | [17]             |
| 46  | Kaempferol                              | A         | $R_1 = R_3 = R_6 = OH, R_2 = R_4 = R_5 = R_7 = H$                                           | S, J, F    | [14]             |
| 47  | Astragalin                              | A         | $R_1 = O-\beta-D-Glc, R_2 = R_4 = R_5 = R_7 = H, R_3 = R_6 = OH$                            | F, S, J    | [14-15]          |
| 48  | Kaempferol-3- <i>O</i> -glucorhamnoside | A         | $R_1 = O-glucuronide, R_2 = R_4 = R_5 = R_7 = H, R_3 = R_6 = OH$                            | S, J, P    | [14, 16]         |
| 49  | Kaempferol-7- <i>O</i> -glucoside       | A         | $R_1 = R_6 = OH, R_2 = R_4 = R_5 = R_7 = H, R_3 = O-Glc$                                    | S, J       | [14]             |
| 50  | Myricetin                               | A         | $R_1 = R_3 = R_5 = R_6 = R_7 = H, R_2 = R_4 = H$                                            | S, J       | [14]             |
| 51  | Quercetin                               | A         | $R_1 = R_3 = R_6 = R_7 = OH, R_2 = R_4 = R_5 = H$                                           | S, J, P    | [14, 18]         |
| 52  | Isoquercitrin                           | A         | $R_1 = O-\beta-D-Glc, R_2 = R_4 = R_5 = R_7 = H, R_3 = R_6 = OH$                            | P, S, J, F | [14-15, 18, 16]  |
| 53  | Quercetin-3- <i>O</i> -rhamnoside       | A         | $R_1 = O-Rha, R_2 = R_4 = R_5 = H, R_3 = R_6 = R_7 = OH$                                    | P          | [16]             |
| 54  | Quercetin-7- <i>O</i> -glucoside        | A         | $R_1 = R_6 = R_7 = OH, R_2 = R_4 = R_5 = H, R_3 = O-Glc$                                    | P          | [16]             |
| 55  | Quercetin-3'- <i>O</i> -glucoside       | A         | $R_1 = R_3 = R_6 = OH, R_2 = R_4 = R_5 = H, R_7 = O-Glc$                                    | P          | [16]             |
| 56  | Rutin                                   | A         | $R_1 = O-rutinose, R_2 = R_4 = R_5 = H, R_3 = R_6 = R_7 = OH$                               | S, J, P, F | [14, 16, 18, 20] |
| 57  | Hyperoside                              | A         | $R_1 = O-\beta-D-Gal, R_2 = R_4 = R_5 = H, R_3 = R_6 = R_7 = OH$                            | S, J, P    | [14, 16]         |
| 58  | Dihydromyricetin                        | B         | –                                                                                           | S, J       | [14]             |
| 59  | Eriodictyol                             | C         | $R_1 = R_2 = R_3 = R_4 = OH$                                                                | S, J       | [14]             |
| 60  | Naringetol                              | C         | $R_1 = R_2 = R_4 = OH, R_3 = H$                                                             | S, J       | [14]             |
| 61  | Naringin                                | C         | $R_1 = R_4 = OH, R_2 = O-\alpha-L-Mal-(1\rightarrow2)-\beta-D-Mal, R_3 = H$                 | P          | [18]             |
| 62  | Liquiritin                              | C         | $R_1 = R_3 = H, R_2 = OH, R_4 = O-\beta-D-Glc$                                              | S, J       | [14]             |
| 63  | Pinocembrin                             | C         | $R_1 = R_2 = OH, R_3 = R_4 = H$                                                             | S, J       | [14]             |
| 64  | Hesperetin                              | C         | $R_1 = R_2 = R_3 = R_4 = OH$                                                                | P          | [18]             |
| 65  | Hesperidine                             | C         | $R_1 = R_2 = R_3 = OH, R_4 = O-rutinose$                                                    | P          | [18]             |
| 66  | Genistein                               | D         | $R_1 = R_2 = H$                                                                             | S, J       | [14]             |
| 67  | Genistin                                | D         | $R_1 = \beta-D-Glc, R_2 = H$                                                                | S, J       | [14]             |
| 68  | Biochanin A                             | D         | $R_1 = H, R_2 = CH_3$                                                                       | F          | [21]             |
| 69  | Naringenin chalcone                     | E         | $R_1 = OH, R_2 = H$                                                                         | S, J       | [14]             |
| 70  | Isoliquiritin                           | E         | $R_1 = H, R_2 = \beta-D-Glc$                                                                | S, J       | [14]             |
| 71  | Phloretin                               | F         | –                                                                                           | S, J       | [14]             |
| 72  | Catechin                                | G         | $R = H$                                                                                     | S, J, P, F | [13-14, 16, 22]  |
| 73  | Gallocatechin                           | G         | $R = OH$                                                                                    | S, J, P    | [13-14]          |
| 74  | Epicatechin                             | H         | $R = H$                                                                                     | S, J, P    | [13-14]          |
| 75  | Epigallocatechin                        | H         | $R = OH$                                                                                    | S, J, P    | [13-14]          |

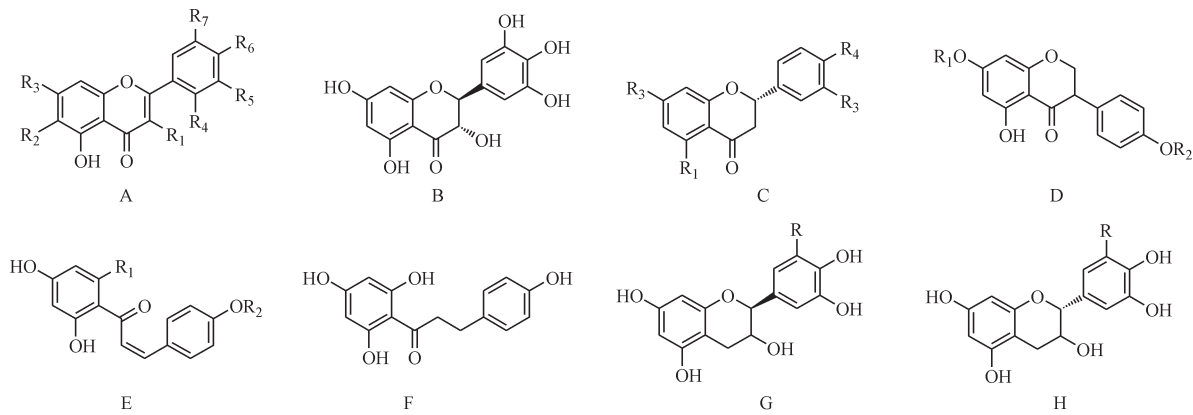


Figure 2 Nuclear structures of flavonoids in different parts of pomegranate

Table 3 Terpenoids in different parts of pomegranate

| No. | Compound           | Part    | Reference |
|-----|--------------------|---------|-----------|
| 76  | Oleuropein         | S, J    | [13]      |
| 77  | Abscisis acid      | S, J    | [13]      |
| 78  | Atractylenolide I  | S, J    | [13]      |
| 79  | $\alpha$ -Cyperone | S, J    | [13]      |
| 80  | Corosolic acid     | S, J    | [13]      |
| 81  | Ursolic acid       | S, J, F | [18, 20]  |
| 82  | Betulonic acid     | S, J    | [13]      |
| 83  | Maslinic acid      | S, J    | [13]      |
| 84  | Oleanolic acid     | S, J, F | [13, 20]  |
| 85  | Taraxerol          | F       | [21]      |

Table 4 Alkaloids in different parts of pomegranate

| No. | Compound              | Part | Reference |
|-----|-----------------------|------|-----------|
| 86  | Trigonelline          | S, J | [13]      |
| 87  | Indigo                | S, J | [13]      |
| 88  | Indirubin             | S, J | [13]      |
| 89  | Palmatine             | S, J | [13]      |
| 90  | Berberine             | S, J | [13]      |
| 91  | Caffeine              | P    | [17]      |
| 92  | Hygrine               | P    | [23]      |
| 93  | Norhygrine            | P    | [23]      |
| 94  | Pseudopelletierine    | P    | [23]      |
| 95  | Norpseudopelletierine | P    | [24]      |
| 96  | Pelletierine          | P    | [24]      |
| 97  | N-Methylpelletierine  | P    | [24]      |

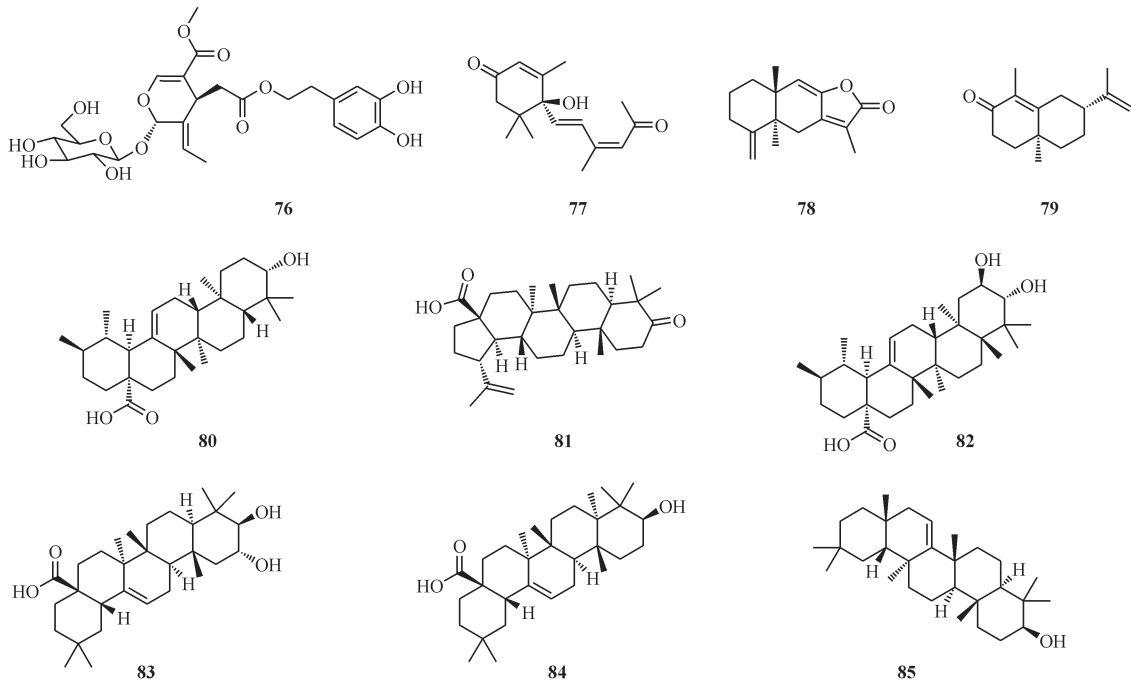


Figure 3 Structures of terpenoids in different parts of pomegranate

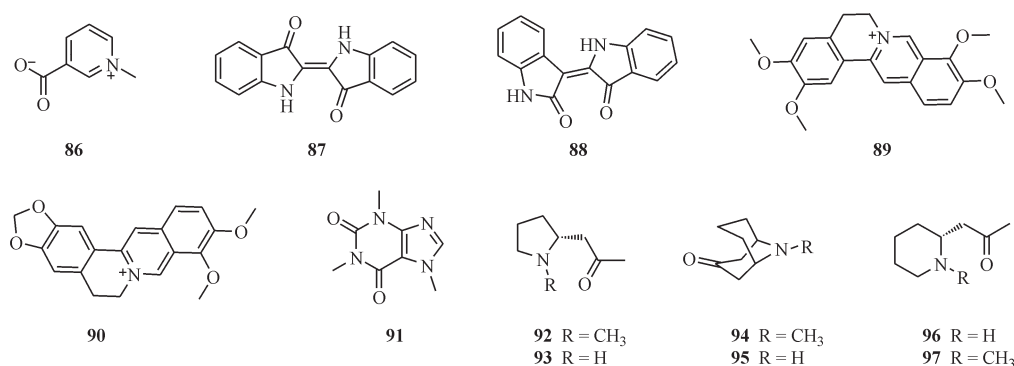


Figure 4 Structures of alkaloids in different parts of pomegranate

Table 5 Phenolic acids in different parts of pomegranate

| No. | Compound                            | Part       | Reference    |
|-----|-------------------------------------|------------|--------------|
| 98  | 2S, 3S, 4S-Trihydroxypentanoic acid | F          | [20]         |
| 99  | Cinnamic acid                       | S, J, P    | [13, 17]     |
| 100 | 4-Hydroxycinnamic acid              | S, J, P    | [13, 17, 22] |
| 101 | Ferulic acid                        | S, J, P    | [13, 17, 22] |
| 102 | Methyl ferulate                     | S, J       | [13]         |
| 103 | Isoferulic acid                     | S, J, P    | [13, 17]     |
| 104 | Sinapic acid                        | S, J       | [13]         |
| 105 | Caffeic acid                        | S, J, P    | [15, 17, 22] |
| 106 | Caffeic acid phenethyl ester        | S, J       | [13]         |
| 107 | Salicylic acid                      | S, J, P    | [13, 17]     |
| 108 | 2, 5-Dihydroxybenzoic acid          | S, J, P    | [13, 17]     |
| 109 | 3, 4-Dihydroxybenzoic acid          | S, J       | [13]         |
| 110 | Vanillic acid                       | P          | [17, 22]     |
| 111 | Brevifolin                          | F          | [14]         |
| 112 | Brevifolincarboxylic acid           | S, J, F    | [13-14]      |
| 113 | Methyl brevifolincarboxylate        | F          | [14]         |
| 114 | Ethyl brevifolincarboxylate         | F          | [14]         |
| 115 | Gallic acid                         | P, S, J, F | [12-14, 20]  |
| 116 | Methyl gallate                      | S, J, P    | [12-13]      |
| 117 | Ethyl gallate                       | F          | [14]         |
| 118 | Ellagic acid                        | S, J, P, F | [12-14, 19]  |
| 119 | Chlorogenic acid                    | P          | [17, 22]     |
| 120 | Rosmarinic acid                     | P          | [22]         |

137)。除此之外, Gómez-Caravaca 等<sup>[16]</sup>通过 HPLC-DAD-ESI-MS 技术发现了石榴汁中还存在花青素-黄烷醇复合型化合物。具体化合物信息见表 6 (121 ~ 137)。

## 2.7 脂肪酸类

目前,从石榴种子、皮、花中已发现了 16 个脂肪酸类化合物<sup>[20,28-30]</sup>,包括 7 个不饱和脂肪酸类,9 个饱和脂肪酸类。石榴种子中富含脂肪酸类化合

Table 6 Anthocyanins in different parts of pomegranate

| No. | Compound                                                  | Part | Reference    |
|-----|-----------------------------------------------------------|------|--------------|
| 121 | Malvidin-3- <i>O</i> -glucoside                           | J    | [25]         |
| 122 | Malvidin-3- <i>O</i> -(6"-acetyl)-glucoside               | P, J | [25]         |
| 123 | Petunidin-3- <i>O</i> -glucoside                          | J    | [25]         |
| 124 | Peonidin-3- <i>O</i> -glucoside                           | P    | [25]         |
| 125 | Peonidin-3- <i>O</i> -(6"-malonyl)-glucoside              | P    | [25]         |
| 126 | Peonidin-3- <i>O</i> -(6"- <i>p</i> -coumaroyl)-glucoside | J    | [25]         |
| 127 | Cyanidin-3- <i>O</i> -galactoside                         | J    | [26]         |
| 128 | Cyanidin-3- <i>O</i> -glucoside                           | J, F | [14, 16, 26] |
| 129 | Cyanidin-3- <i>O</i> -rutinoside                          | J    | [16]         |
| 130 | Cyanidin-3,5- <i>O</i> -diglucoside                       | J, F | [14, 16, 26] |
| 131 | Delphinidin-3- <i>O</i> -glucoside                        | J, F | [14, 16, 26] |
| 132 | Delphinidin-3- <i>O</i> -caffeoyl                         | J    | [26]         |
| 133 | Delphinidin-3,5-diglucoside                               | J    | [16, 27]     |
| 134 | Delphinidin-3- <i>O</i> -caffeoyl-5- <i>O</i> -glucoside  | J    | [26]         |
| 135 | Pelargonidin-3- <i>O</i> -glucoside                       | J, F | [14, 16, 27] |
| 136 | Pelargonidin-3- <i>O</i> -caffeoyl-5- <i>O</i> -glucoside | J    | [26]         |
| 137 | Pelargonidin-3, 5-diglucoside                             | J, F | [14, 16, 27] |

物,石榴籽油主要由不饱和脂肪酸组成,石榴酸(punicic acid)是石榴籽油中主要脂肪酸,有研究通过 GC-MS 法测定其含量为 74% ~ 85%<sup>[28,31]</sup>。

## 2.8 其他类

除上述化学成分外,石榴种子、汁、花中还存在甾醇类化合物<sup>[20-21,27]</sup>。经 LC-MS 分析,石榴籽中存在核苷类、香豆素类、醌类化合物<sup>[13]</sup>。此外,Ito 等<sup>[18]</sup>在石榴假种皮中分离得到了 1 个新的木脂素类化合物 pomegralignan。

## 3 药理活性

现代药理研究表明,石榴各药用部位具有抗氧化、降血糖、抗炎、抗动脉粥样硬化作用、抗肿瘤作用、抗菌作用等。



### 3.1 抗氧化作用

Chang等<sup>[32]</sup>发现石榴皮中所含的安石榴苷(punicalagin)具有较好的清除DPPH(1,1-二苯基-2-三硝基苯肼)自由基和 $\cdot\text{OH}$ 的能力,  $\text{IC}_{50}$ 分别为101.0和227.0  $\mu\text{g/mL}$ 。Zu等<sup>[33]</sup>发现石榴皮超微粉可以显著提高大鼠血清中超氧化物歧化酶(SOD)、过氧化氢酶(CAT)和谷胱甘肽过氧化物酶(GSH-PX)的活力,并有效减少血清中丙二醛(MDA)的量,提高大鼠体内血清的抗氧化能力。实验研究表明,石榴皮80%乙醇提取物的抗氧化活性和总酚、总黄酮和黄酮醇的含量均高于种子和果汁,进一步分析表明,其抗氧化活性与总酚含量呈显著正相关<sup>[34]</sup>。Yoshime等<sup>[35]</sup>发现石榴籽油对DPPH自由基和ABTS(2,2'-联氮-双-3-乙基苯并噻唑啉-6-磺酸)自由基的清除作用与其浓度呈正相关,  $\text{EC}_{50}$ 分别为8.8和5.9  $\text{mg/mL}$ 。Xing等<sup>[36]</sup>发现石榴叶多酚对亚硝酸盐、超氧阴离子自由基、 $\cdot\text{OH}$ 均具有清除作用,其清除率与提取物浓度和纯度呈正相关。

### 3.2 抗糖尿病作用

Liu等<sup>[37]</sup>发现石榴皮中安石榴苷可与 $\alpha$ -葡萄糖苷酶结合形成酶-抑制物(EI)复合体,同时,安石榴苷还可以与EI复合体结合,进而形成酶-底物-抑制物复合体,其对 $\alpha$ -葡萄糖苷酶有抑制作用。Kam等<sup>[38]</sup>发现石榴花甲醇提取物体外抑制 $\alpha$ -淀粉酶和 $\alpha$ -葡萄糖苷酶活性,而石榴皮甲醇提取物选择性抑制 $\alpha$ -葡萄糖苷酶活性,除此之外,没食子酸和鞣花酸也表现出对 $\alpha$ -葡萄糖苷酶的选择性抑制。Zhang等<sup>[39]</sup>发现石榴皮多酚能够改善氧化应激并促进转录因子FoxO1向细胞核外的易位,使胰岛素合成增加,从而治疗高脂饮食和链脲佐菌素(STZ)诱导的大鼠胰腺组织损伤和胰岛素分泌不足。实验研究表明,市售石榴果实提取物、安石榴苷和鞣花酸通过清除甲基乙二醛抑制AGEs(晚期糖基化终末产物)显示出比阳性对照二甲双胍更强的体外抗糖基化作用<sup>[40]</sup>。Gósciniak等<sup>[41]</sup>发现石榴花提取物具有抑制 $\alpha$ -淀粉酶和 $\alpha$ -葡萄糖苷酶的功效,该提取物抑制 $\alpha$ -葡萄糖苷酶的能力优于阿卡波糖,而抑制 $\alpha$ -淀粉酶的能力弱于阿卡波糖。

### 3.3 抗炎作用

Wu等<sup>[42]</sup>发现在DDS(4,4'-二氨基二苯砜)诱导的小鼠炎症模型中,石榴汁显著降低促炎因子IL-1 $\beta$ 、IL-6、TNF- $\alpha$ 、IFN- $\gamma$ 的表达,增加抗炎因子表

达,并可降低氧化应激水平及炎症标志物MPO(髓过氧化物酶)水平,从而改善因炎症反应造成的结肠上皮结构损伤。Lee等<sup>[43]</sup>发现石榴中安石榴苷、安石榴林(punicalin)和石榴皮素B(granatins B)在脂多糖(LPS)诱导的RAW 264.7巨噬细胞中抑制NO的产生和诱导型一氧化氮合酶(iNOS)的表达,显著降低了LPS诱导的小鼠足趾肿胀。Marques等<sup>[44]</sup>发现石榴叶70%乙醇提取物降低LPS诱导急性腹膜炎大鼠体内TNF- $\alpha$ 水平并减少大鼠腹膜白细胞数量,发挥抗炎作用。

### 3.4 抗动脉粥样硬化作用

Benchagra等<sup>[45]</sup>发现石榴皮、石榴假种皮70%甲醇提取物均显著增加血浆血清对氧磷酶(PON1)的活性和PON1蛋白表达,还可以通过抑制脂蛋白氧化、减少过氧化氢含量,以此预防动脉粥样硬化和心血管疾病的发生。Anwaier等<sup>[46]</sup>发现石榴皮60%乙醇提取物安石榴苷通过抑制低振荡剪切应激(OSS)诱导的大鼠主动脉狭窄后区域的内皮细胞中Smad1/5的活化改善其功能障碍。此外,实验研究表明,石榴皮乙醇提取物和安石榴苷能抑制促炎刺激下大鼠血管平滑肌细胞的增殖,从而抑制动脉粥样硬化。Aharoni等<sup>[47]</sup>发现石榴汁及其多酚剂量依赖性地抑制巨噬细胞炎症反应,并促进巨噬细胞由M1促炎表型向M2抗炎表型转变,石榴汁摄入可能抑制主动脉中进行性促炎状态以及动脉粥样硬化的发展。

### 3.5 抗肿瘤作用

Benchagra等<sup>[45]</sup>发现石榴皮、石榴籽70%甲醇提取物均能降低J82人膀胱癌细胞中硫代巴比妥酸活性物质含量,且以剂量依赖的方式显著降低J82细胞中活性氧(ROS)产生,抑制了应激状态下J82细胞的脂质过氧化。Eskandari等<sup>[48]</sup>发现鞣花酸剂量依赖性地增加人前列腺癌细胞(PC3)中IL-6基因表达和其分泌水平,并减少STAT3(signal transducer and activator of transcription 3)、ERK(extracellular signal-regulated kinase)等细胞信号蛋白磷酸化,从而减少细胞增殖。Mandal等<sup>[49]</sup>发现石榴乳剂下调DMBA(7,12-二甲基苯并[ $\alpha$ ]蒽)诱导的大鼠乳腺肿瘤中 $\alpha$ 雌激素受体(ER- $\alpha$ )、 $\beta$ 雌激素受体(ER- $\beta$ )和细胞周期蛋白D1的过度表达,降低ER- $\alpha$ /ER- $\beta$ 的比值以及 $\beta$ -连环蛋白的表达水平,同时阻断细胞质积累和核易位而发挥其抗肿

瘤细胞增殖和促凋亡作用。

### 3.6 抗菌作用

Song等<sup>[50]</sup>发现石榴皮鞣质对革兰阳性菌具有较强的抗菌作用,实验研究表明,石榴皮鞣质能够抑制菌体蛋白质合成,其通过破坏菌体的细胞壁和细胞膜结构,改变菌体正常的渗透性抑制金黄色葡萄球菌(*S. aureus*)。实验研究表明,石榴皮70%甲醇粗提取物对黄曲霉(*A. flavus*)、轮枝镰孢菌(*F. verticillioides*)、霉心病菌(*A. alternata*)和灰霉菌(*B. cinerea*)的生长有抑制作用,且提取物中鞣花酸含量对其抗菌活性有显著影响<sup>[51]</sup>。Gullon等<sup>[52]</sup>发现石榴皮生药粉对单核细胞增生李斯特菌(*L. monocytogenes*)、李斯特菌(*L. innocua*)、金黄色葡萄球菌、铜绿假单胞菌(*Pseudomonas aeruginosa*)、大肠埃希菌(*Escherichia coli*)和沙门氏菌(*Salmonella*)均有抗菌活性,最低抑菌浓度为20 mg/mL至50 mg/mL不等。Wu等<sup>[53]</sup>发现石榴花乙醇提取物能够抑制变形链球菌(*S. mutans*)的生长,且抑菌能力与提取物浓度呈正相关,提示石榴花提取物的抑菌作用与其多酚成分有关。

### 3.7 其他作用

(1)驱虫作用:Meng<sup>[54]</sup>发明了一种含有石榴根皮的中药组合物,具有预防和治疗胆道蛔虫、带绦虫或绦虫感染引起的急性慢性胆囊炎作用。(2)促进脂质代谢:Kearns等<sup>[55]</sup>发现安石榴苷通过活化AMPK/ACC途径减少脂肪生成,加速脂肪降解,从而改善高脂饮食诱导的肥胖小鼠肝脏脂质沉积。(3)抗病毒作用:Salles等<sup>[56]</sup>发现石榴皮乙醇提取物及富含安石榴苷的流份具有抗马雅罗(Mayaro)病毒活性,实验研究表明,石榴叶乙醇提取物具有显著的抗马雅罗病毒活性,约为98%。

## 4 结语与展望

石榴药材资源丰富、应用广泛,其果皮、种子、花、叶、根均可入药,但中药和民族药对石榴的应用存在差异。首先,中药主要以石榴皮作为药用部位<sup>[5]</sup>,而民族药对石榴籽、花、根等药用部位应用广泛。其次,藏医和蒙医应用石榴治疗消化不良、胃炎等疾病<sup>[6,9]</sup>,而中医相关应用很少。石榴各药用部位主要化学成分包括鞣质类、酚酸类、黄酮类等,具有抗氧化、抗炎、降血糖等多种药理作用。石榴具有涩肠止泻功效,可用于治疗腹泻、痢疾

等,腹泻的常见病因包括细菌感染、肠道炎症等<sup>[57]</sup>,同时现代药理学研究发现石榴具有抗炎抗菌作用,表明中药传统功效与现代药理作用之间存在一定关联<sup>[58-59]</sup>。

近年来国内外对石榴各药用部位的研究主要集中于石榴皮、籽、花,而对石榴叶和根的研究较少;另一方面,尽管石榴多样的药理活性已得到广泛验证,但大多研究应用混合提取物验证其治疗作用,对单体化合物的活性研究较少。此外,对石榴各药用部位的药理活性研究多为体外筛选,其药效物质与作用机制的关系有待更深层次的探索。本文对石榴各药用部位的民族药用法、化学成分及药理作用进行综述,以期阐明其药效物质基础提供科学依据,为其进一步综合利用提供参考。

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