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Recent studies on antimicrobial and anticancer activities of saponins: a mini-review

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ABSTRACT

Multidrug-resistant cancer cells and microbial pathogeneses remain the complicated hindrances in therapy for cancer and microbial infections. In addition, severe side effects from chemotherapy can result from conventional drugs. New formulations based on bioactive compounds isolated from medicinal plants may alleviate these side effects and increase antimicrobial activity. Saponins as surface-active triterpene glycosides can be synthesized by various plants (wild plants and cultivated crops such as soapbark trees and soapwort), lower marine animals, and some bacteria. Nano-formulations of saponins, particularly on a scale of <100 nm, can augment therapeutic effects in the body by overcoming some disadvantages of saponins, mainly potential damage to the intestinal mucosa and disruption of blood cells.

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1. Introduction

Inactivation and eradication of microbial pathogens and cancer cells by current formulations are complicated issues due to their drug resistance [1-3]. Saponins are surface-active triterpene glycosides synthesized by various plant species (wild plants and cultivated crops), lower marine animals, and some bacteria [4, 5]. These compounds have bitter-tasting and foamy quality in an aqueous medium (the amphipathic helpful featureuses a natural surfactant [6]) with widely distributed in soapbark tree (*Quillaja saponaria*) and soapwort (genus *Saponaria*) [7]. The main biomedical, nutraceutical, and industrial applications for saponins such as glycyrrhizin, licorice flavoring (natural flavoring extract), and quillaia (the milled inner bark of the soapbark (*Quillaja saponaria*) involve the production of soaps, fire extinguishers, dietary supplements, steroids and used in carbonated beverages. Antioxidant potential in brain mitochondria, hypolipidemic (lipid-lowering agents), anticancer activity (induction of apoptosis and suppression of metastasis), hepatoprotective, haemolytic, anti-inflammatory, antibacterial, antiviral [8, 9], antifungal [10], and anti-ulcer, and the anti-diabetic properties through augmenting in an expression of adipsin and activation of adenosine monophosphate-activated protein kinase (AMPK) [11], activation of peroxisome proliferator-activated receptors gamma (PPARγ), activation of glucose transporter type 4 (Glut4), activation of adiponectin expression, activation of PI3K/Akt pathway. As the main pharmaceutical applications, antimicrobial (Table 1) and anticancer (Figure 1 and Table 2) activities of the significant saponins have been discussed in this letter. Interestingly, nano-formulations of these compounds, specifically in the scale of 1-100 nm can increase therapeutic effects in physiological conditions with overcoming some disadvantages of saponins mainly potential damage to intestinal mucosa and disrupting erythrocytes [12-16].

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Table 1. The major saponins with antimicrobial activities.

Names	Chemical formula	Antimicrobial activities	Ref.
Glycyrrhizin (the sapogenin moiety)	$C_{42}H_{62}O_{16}$	Anti-coronavirus against severe acute respiratory syndrome coronavirus 2 (SARS‑CoV‑2) by binding to the angiotensin-converting enzyme 2 (ACE2) receptor, hindering the SARS-CoV-2 from entering to new cells.	[8]
Quillaja saponin-stabilized carvacrol nanoemulsions (average droplet diameters < 150 nm)	$C_{36}H_{54}O_{11}$	Antibacterial effect on *Salmonella enterica*, electrostatic interaction between the cationic microemulsion and the anionic bacteria membranes (the presence of anionic lipopolysaccharides) resulted in increased cell membrane permeability.	[17]
N-hydroxyacyl and N-aminoacyl derivatives of diosgenyl 2-amino-2-deoxy-β-d-glucopyranoside (a synthetic saponin)	$C_6H_{13}NO_5$ for 2-amino-2-deoxy-alpha-D-glucopyranose	α-amino group in aminoacyl residue led to significant antimicrobial activities of the saponins against *Candida albicans*, *Candida lipolytica*, *Bacillus subtilis*, *Enterococcus faecalis*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*	[18]

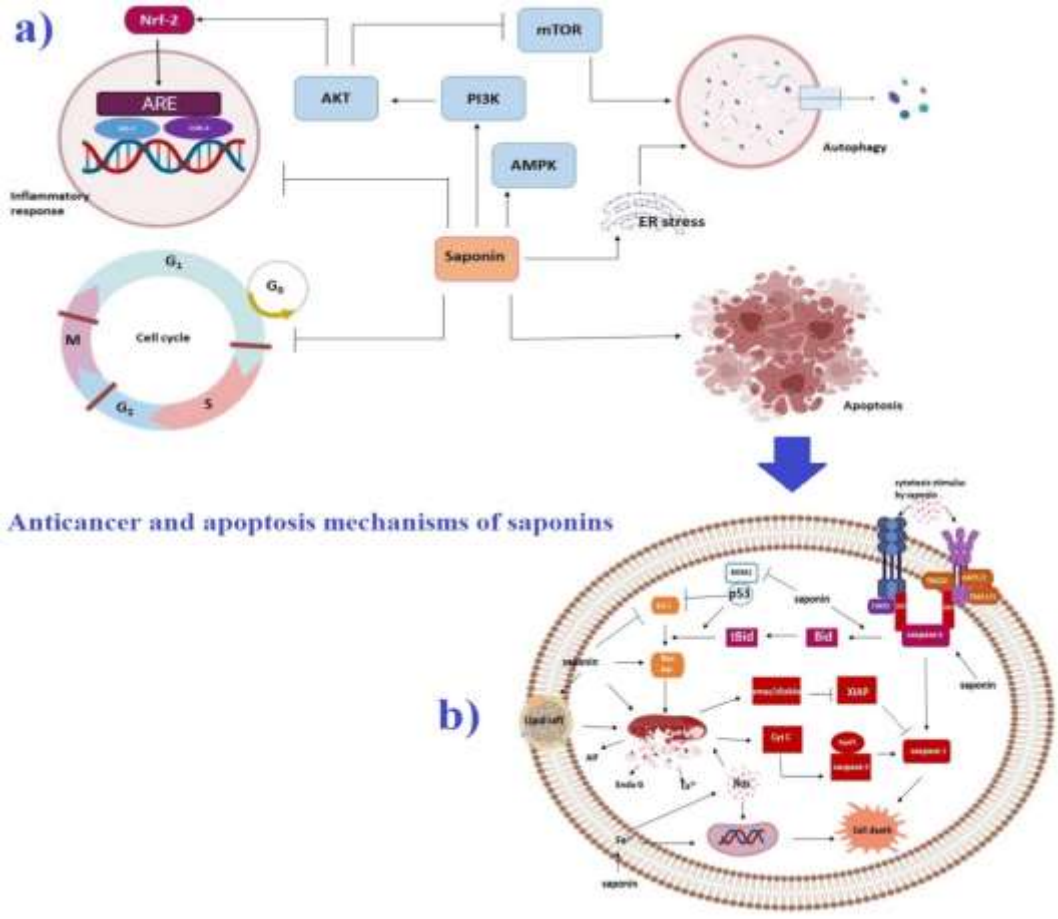

Fig. 1. Anticancer (a) and apoptosis (b) mechanisms for saponins [19].

Table 2. The major saponins with anticancer activities.

Names	Chemical formula	Anticancer activities	Ref.
Asparanin A (a steroidal saponin)	$C_{39}H_{64}O_{13}$	Anticancer effect on endometrial cancer by induction of apoptosis and autophagy processes via endoplasmic reticulum stress and DNA damage.	[20]
Platycodin D (a terpenoid saponin)	$C_{57}H_{92}O_{28}$	Anticancer activity results from promoting the extracellular release of the immune checkpoint glycoprotein PD-L1 (programmed death-ligand 1) by a function of metalloproteases and a cholesterol-binding-related effect.	[21]
Gracillin (natural steroidal saponin)	$C_{45}H_{72}O_{17}$	Induction of apoptosis in HL60 human leukemia cell line through cell cycle arrest of G1 and oxidative stress. Additionally, the blockage of mitochondrial complex II-mediated energy production, targeting both oxidative phosphorylation (OXPHOS) and glycolysis (targeting of phosphoglycerate kinase 1 (PGK1)) have been found in the case of non-small cell lung cancer (NSCLC) and breast cancer cells, respectively.	[22-24]
Pulsatilla saponin D (hederacolchiside A; SB365)	$C_{47}H_{76}O_{17}$	Apoptosis activator through promoting caspase-independent cell death in glioblastoma multiforme cells.	[25]
Raddeanin A (triterpenoid saponin)	$C_{47}H_{76}O_{16}$	Inhibition of osteosarcoma in metastasis stage via suppressing matrix metalloproteinase-2/9 (MMP-2/9) expression and blockage of IκBα (nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha) phosphorylation for inactivation of NF-κB signal pathway.	[26]

2. Conclusions

New formulations based on bioactive compounds such as saponins isolated from medicinal plants can be used to overcome multidrug resistance in cancer cells and microbial pathogeneses as well as severe side effects of chemotherapy. In this way, nano-formulations of saponins, particularly on a scale of <100 nm, can augment antimicrobial and anticancer activities in physiological conditions by overcoming some disadvantages of saponins, such as potential damage to the intestinal mucosa and disrupting blood cells. Disruption of bacterial cell walls and membranes has been found for nano-formulations of saponins. In the case of anticancer mechanisms, apoptosis induction and inhibition of metastasis stage via suppressing MMP-2/9 in several types of cancers have been reported for these formulations. However, the biocompatibility, biodegradability, and bioavailability of these formulations should be evaluated in future investigations.

Study Highlights

- Nano formulations based on saponins can be applied to overcome multidrug resistance in cancer cells and microbial pathogeneses as well as severe side effects of chemotherapy.
- Disruption of bacterial cell walls and membranes has been found for nano-formulations of saponins.
- In the case of anticancer mechanisms, apoptosis induction and inhibition of metastasis stage via suppressing MMP-2/9 in several types of cancers have been reported for these formulations.
- The biocompatibility, biodegradability, and bioavailability of these formulations should be evaluated in future investigations.

Abbreviations

ACE2: The angiotensin-converting enzyme 2
AMPK: Adenosine monophosphate-activated protein kinase
Glut4: Glucose transporter type 4
IκBα: Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha
MMP-2/9: Matrix metalloproteinase-2/9
NSCLC: Non-small cell lung cancer
OXPHOS: Oxidative phosphorylation
PD-L1: Programmed death-ligand 1
PGK1: Phosphoglycerate kinase 1
PPARγ: Peroxisome proliferator-activated receptors gamma
SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

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Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

This article does not contain any studies with animals or human participants performed by any of the authors.

Authors' contribution

Both authors: conceptualization, preparing the first drafting, and revising the manuscript.

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References

1.Amraei S, Eslami G, Taherpour A, Hashemi A. Relationship between MOX genes and antibiotic resistance in Klebsiella pneumoniae strains in nosocomial infections. Micro Nano Bio Aspects. 2022;1(2):12-7
2.Amraei S, Eslami G, Taherpour A, Hashemi A. The role of ACT and FOX genes in Klebsiella pneumoniae strains isolated from hospitalized patients. Micro Nano Bio Aspects. 2022;1(2):18-25
3.Alavi M, Webster TJ, Li L. Theranostic safe quantum dots for anticancer and bioimaging applications. Micro Nano Bio Aspects. 2022;1(2):1-11
4.Yatham P, Dahat Y, Khan A, Baishya R, Srivastava AK, Kumar D. Saponin Stabilized Emulsion as Sustainable Drug Delivery System: Current Status and Future Prospects. Nanopharmaceutical Advanced Delivery Systems2021. p. 217-35. doi:https://doi.org/10.1002/9781119711698.ch10
5.Ahmadi S, Ahmadi G, Ahmadi H. A review on antifungal and antibacterial activities of some medicinal plants. Micro Nano Bio Aspects. 2022;1(1):10-7
6.Sochacki M, Vogt O. Triterpenoid Saponins from Washnut (Sapindus mukorossi Gaertn.)—A Source of Natural Surfactants and Other Active Components. Plants. 2022;11(18):2355. doi:https://doi.org/10.3390/plants11182355
7.Bezerra KGO, Rufino RD, Luna JM, Sarubbo LA. Saponins and microbial biosurfactants: Potential raw materials for the formulation of cosmetics. Biotechnology Progress. 2018;34(6):1482-93. doi:https://doi.org/10.1002/btpr.2682
8.Bailly C, Vergoten G. Glycyrrhizin: An alternative drug for the treatment of COVID-19 infection and the associated respiratory syndrome? Pharmacology & Therapeutics. 2020;214:107618. doi:https://doi.org/10.1016/j.pharmthera.2020.107618
9.Sharma P, Tyagi A, Bhansali P, Pareek S, Singh V, Ilyas A, et al. Saponins: Extraction, bio-medicinal properties and way forward to anti-viral representatives. Food and Chemical Toxicology. 2021;150:112075. doi:https://doi.org/10.1016/j.fct.2021.112075
10.Morcia C, Piazza I, Ghizzoni R, Delbono S, Felici B, Baima S, et al. In Search of Antifungals from the Plant World: The Potential of Saponins and Brassica Species against Verticillium dahliae Kleb.

Horticulturae. 2022;8(8):1-16. doi:https://doi.org/10.3390/horticulturae8080729
11.Lu JM, Wang YF, Yan HL, Lin P, Gu W, Yu J. Antidiabetic effect of total saponins from Polygonatum kingianum in streptozotocin-induced daibetic rats. J Ethnopharmacol. 2016;179:291-300. doi:https://doi.org/10.1016/j.jep.2015.12.057
12.Pereira GM, Ribeiro MG, da Silva BP, Parente JP. Structural characterization of a new steroidal saponin from Agave angustifolia var. Marginata and a preliminary investigation of its in vivo antiulcerogenic activity and in vitro membrane permeability property. Bioorganic & Medicinal Chemistry Letters. 2017;27(18):4345-9. doi:https://doi.org/10.1016/j.bmcl.2017.08.026
13.Oleszek M, Oleszek W. Saponins in Food. In: Xiao J, Sarker SD, Asakawa Y, editors. Handbook of Dietary Phytochemicals. Singapore: Springer Singapore; 2020. p. 1-40. doi:https://doi.org/10.1007/978-981-13-1745-3_34-1
14.Rejinold NS, Muthunarayanan M, Muthuchelian K, Chennazhi KP, Nair SV, Jayakumar R. Saponin-loaded chitosan nanoparticles and their cytotoxicity to cancer cell lines in vitro. Carbohydrate Polymers. 2011;84(1):407-16. doi:https://doi.org/10.1016/j.carbpol.2010.11.056
15.Jangra S, Sharma B, Jangra R, Chhokar V, Duhan S. Saponin-loaded SBA-15: release properties and cytotoxicity to Panc-I cancer cells. Journal of Porous Materials. 2018;25(4):945-53. doi:https://doi.org/10.1007/s10934-017-0506-y
16.Cibulski S, de Souza TA, Raimundo JP, Nascimento YM, Abreu LS, Suarez N, et al. ISCOM-Matrices Nanoformulation Using the Raw Aqueous Extract of Quillaja lancifolia (Q. brasiliensis). BioNanoScience. 2022. doi:https://doi.org/10.1007/s12668-022-01023-8
17.Ryu V, McClements DJ, Corradini MG, Yang JS, McLandsborough L. Natural antimicrobial delivery systems: Formulation, antimicrobial activity, and mechanism of action of quillaja saponin-stabilized carvacrol nanoemulsions. Food Hydrocolloids. 2018;82:442-50. doi:https://doi.org/10.1016/j.foodhyd.2018.04.017
18.Grzywacz D, Paduszyńska M, Norkowska M, Kamysz W, Myszka H, Liberek B. N-Aminoacyl and N-hydroxyacyl derivatives of diosgenyl 2-amino-2-deoxy-β-d-glucopyranoside: Synthesis, antimicrobial and hemolytic activities. Bioorganic & Medicinal Chemistry. 2019;27(20):114923. doi:https://doi.org/10.1016/j.bmc.2019.05.036
19.Elekofehinti OO, Iwaloye O, Olawale F, Ariyo EO. Saponins in Cancer Treatment: Current Progress and Future Prospects. Pathophysiology. 2021;28(2):250-72.
20.Zhang F, Zhang Y-Y, Ma R-H, Thakur K, Han J, Hu F, et al. Multi-omics reveals the anticancer mechanism of asparagus saponin-asparanin A on endometrial cancer Ishikawa cells. Food & Function. 2021;12(2):614-32. doi:https://doi.org/10.1039/D0FO02265A
21.Bailly C, Vergoten G. Proposed mechanisms for the extracellular release of PD-L1 by the anticancer saponin platycodin D. International Immunopharmacology. 2020;85:106675. doi:https://doi.org/10.1016/j.intimp.2020.106675
22.Min H-Y, Pei H, Hyun SY, Boo H-J, Jang H-J, Cho J, et al. Potent Anticancer Effect of the Natural Steroidal Saponin Gracillin Is Produced by Inhibiting Glycolysis and Oxidative Phosphorylation-Mediated Bioenergetics. Cancers. 2020;12(4):1-20. doi:https://doi.org/10.3390/cancers12040913
23.Chen CR, Zhang J, Wu KW, Liu PY, Wang SJ, Chen DY, et al. Gracillin induces apoptosis in HL60 human leukemic cell line via oxidative stress and cell cycle arrest of G1. Pharmazie. 2015;70(3):199-204
24.Min H-Y, Jang H-J, Park KH, Hyun SY, Park SJ, Kim JH, et al. The natural compound gracillin exerts potent antitumor activity by targeting mitochondrial complex II. Cell Death & Disease. 2019;10(11):1-18. doi:https://doi.org/10.1038/s41419-019-2041-z
25.Hong J-M, Kim J-H, Kim H, Lee WJ, Hwang Y-i. SB365, Pulsatilla Saponin D Induces Caspase-Independent Cell Death and Augments the Anticancer Effect of Temozolomide in Glioblastoma Multiforme Cells. Molecules. 2019;24(18):3230. doi:https://doi.org/10.3390/molecules24183230
26.Ma B, Zhu J, Zhao A, Zhang J, Wang Y, Zhang H, et al. Raddeanin A, a natural triterpenoid saponin compound, exerts anticancer effect on human osteosarcoma via the ROS/JNK and NF-κB signal pathway. Toxicology and Applied Pharmacology. 2018;353:87-101. doi:https://doi.org/10.1016/j.taap.2018.05.025

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