Review Article

Cucurbita pepo and Cucurbitacin in the Management of Anti-proliferation by JAK/STAT Pathway

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ABSTRACT

Pumpkin *(Cucurbita pepo)* is capaciously recycled similar to food and in folk medicine throughout the world. It accords to genus Cucurbita (C_{CT}) under family Cucurbitaceae. There are a plenty of important medicinal phyto-constituents belonging to cucurbitoside like triterpenoids, C^{AR}_{T} and C_{CT} glycosides. A survey of the literature demonstrates that *C. pepo*, has the capacity to improve prostatic hyperplasia, urinary dysfunction and cytotoxic properties. Many pharmacological revisions have established its role in hepatoprotection, inhibition of P_r^{st} gland cancer (C_{NCR}), anti (A^n_t) oxidant effects, inhibition of L_u^G, B_R^{st} and triple-negative B_R^{st} C_{NCR} by blocking JAK/STAT signaling (S_{gls}) pathway (P_{tw}). It has also A^n_t microbial, A^n_t -inflammatory, A^n_t -diabetic and A^n_t ulcer activities by supporting its traditional claims. Establishment of *C. pepo* and cucurbitacin (C_{CBT}) in the management of A^n_t -proliferation by JAK/STAT P_{tw}. Data towards writing this review are generated through exploration of different websites like MEDLINE (PubMed), Google Scholar, Science Direct, Scopus, Cochrane, SID and Magiran databases. We have selected 2016-2018 duration for the same purpose. We have found 88 papers related to this topic. C_{CBT} is found to arrest unlimited cell (C_{EL}) division and respective apoptosis (A_{ppt}) *in vitro* and *in vivo* C_{NCR} models. A plenty of molecular design targeting C_{CBT} have been invented, such as fibrous-actin, S_{gls} transducer and activator of transcription (STAT), cyclooxygenase-2, etc. This review is minded at C_{CBT} from *C. pepo* which dwindle the proliferation of human C_{NCR} C_{EL} through the JAK/STAT P_{tw}.

Key words: Anticancer activity, *Cucurbita pepo*, Cucurbitaceae family, JAK/STAT pathway, Cucurbitacin, Cyclooxygenase-2.

INTRODUCTION

C_{NCR} lies its uniqueness to the maximum normally identified diseases (D_{SEAS}) and is associated with ill health and death set up causing a health problem globally. Even though unlimited determinations have been found ready to find out a remedy, C_{NCR} remnants a very projecting cause of death in humans. Carcinogenesis (C_{CNG}) is a different step and different factorial process including the incidence of vibrant and disconnected molecular and C_{EL} modifications. There are different but thoroughly associated stages of origination, elevation and development are found in C_{NCR}.[1] Present-day C_{NCR} treatments, chemotherapy, targeted agents, radiation, surgery and immunosuppression have restrictions subsequent from the expansion of resistance to the treatment. The identification of defensive molecules starved of side effects ruins a crucial independent in the fight against C_{NCR}. The additional choices goal next to the initial finding of C_{NCR} in the preliminary stage can assist with its appropriate supervision. In the meantime, plant (P_{Lt})-derived products have taken a major role to inhibit numerous chronic D_{SEAS}, as well as C_{NCR}. The use of P_{Lt} substances to inhibit or defer the growth of C_{CNG} has been called for chemoprevention and there is a rapid increasing attention towards the usage of natural compounds as probable chemo-protective and therapeutic

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agents.[2] Pumpkin (P_{MPN}) seed (S_{Ed}) has several health benefits. P_{MPN} is refined all over the biosphere for usage as root vegetables as well as medicine.[3] It is also recycled by tradition as medicine in many nation-states such as China, Yugoslavia, Argentina, India, Mexico, Brazil and America. Its extensively detained medicinal (M_{edc}) usages have concentrated investigation with modern implements and recognized with good A^n_t -diabetic, A^n_t -hypertension, A^n_t –tumor(t^m_R), immunomodulation, A^n_t bacterial, A^n_t -hypercholesterolemia, intestinal A^n_t -parasitic, A^n_t -inflammatory and analgesic properties.[4]

Cucurbita pepo

P_{MPN} (*Cucurbita pepo*) is one of the eldest identified nurtured classes of shrub. It accords to the genus C_{CT} and family Cucurbitaceae or C_{CT} and contain crops like cucumbers. Ethno-pharmacological studies display that *C. pepo* is recycled in various countries for treating many D_{SEAS} like inflammation, viral infections, pain, urinary disorders, ulcer, diabetes and oxidation.[5] Mainly Ayurveda system has used to assess segment of the P_{Lt} as well as corpuscles of the fruits ($_{Fr}^{ut}$) and S_{Ed}. The S_{Ed} are recycled to treat the problems of urinary system, hypertension, kidney stones, prostate (P^{st}_r) D_{SEAS}, erysipelas skin ($^{Sk}_N$) infection and carcinomas (C_{Arom}). Exact cultivars of winter squash resulting from other species such as *C. argyrosperma* and *C. moschata*, are also at times called " P_{MPN}.[6]

Taxonomical Classification of *C. pepo*

Taxonomic classification.[7]

Kingdom: Plantae
Subkingdom: Tracheobionta
Super division: Spermatophyta
Division: Magnoliopsida
Subclass: Dileniidae
Order: Violales
Family: Cucurbitaceae
Genus: C_{CT} L
Species: C_{CT} *pepo* L

Vernacular Names

Hindi: Safed Kaddu, Kumrha Marathi: Kohala, Bhopli Telugu: budadegummadi, Bengali: Safed Kaddu, Sanskrit: karkaru, kurkaru and kurlaru, kushmanda English: squash.[8,9]

Habitat

P_{MPN} are full-fledged throughout the biosphere for a diversity of explanations extending from agronomic ulterior motive. Only Antarctica is not capable to harvest $P_{MPN.}$ The major international manufacturers of P_{MPN} consist of the United States, Canada, Mexico, India and China.[10]

Plant Characteristics

P_{MPN} is yearly parsley with heavy mounting stems. The root is thriving established and towards 40 cm unfathomable with 5m extended. The stems are a branch off, enclosed in spongy white up to 10 m long and frequently yield extrinsic roots at nodes. The petioles are 5-20 cm long. The tinny leaves are alternative, modest, palmate, veined, round to reniform, essentially cordate, apically obtuse, unsubdivided to trivial 5-7 lobed, 7-30 cm across, wide-ranging than long, stark to soft blooming and finely margin with toothlike projection, 3-5 rounded or obtuse, apiculate lobules, the central one bigger than lateral ones.[11,12] Unisexual flowers of P_{MPN} are aromatic. The calyx is enclosed in white pubescence and bears 5 free sepals, 0.5-2 cm long. The corolla is yellow to orange color, tubular at least 5 cm long and broad. Staminate flowers are about 10-23 cm long. Pistillate flowers are grown on shorter pedicles, only up to 5.5 cm long and have an inferior 1- ocular ovoid ovary with a short thick style with 3-5 bilobed stigmas. $_{Fr}^{ut}$ are are highly inconstant in shape, color and size.[13] The shape is elongated, cylindrical, oval, flattened, globular, heart-shaped and tapering to a curved neck on one or both ends. The length is from 5.8 to 71.6 cm and width from 11.2 to 48.6 cm. The $^{Sk}_N$ can be smooth, wrinkled. The flesh, variable in color and thickness can be white, yellow, or orange and 1 to 6.4 cm thick[14] [Figure 1].

S_{Ed} *Characteristics*

P_{MPN} S_{Ed} is also recognized as pepita. The S_{Ed} are characteristically flat, unequally oval, light green in color and typically enclosed by a white husk [Figure 2].[15] P_{MPN} S_{Ed} produce 34-54% oil. The size and weight of the S_{Ed} rise as the $_{Fr}^{ut}$ size rises, lining up between 1.6 to 2.9 cm long, 0.7 to 1.6 cm wide and 0.28 to 0.69 cm thick. The S_{Ed} seem doable for 6-8 years but abide by no endosperm and the embryo embody leaf-like cotyledons and a short radicle.[16] P_{MPN} S_{Ed} oil is popular as succulent oil and also used as a nutritious food. P_{MPN} S_{Ed} and its oil are prosperous in phytosterols, polyunsaturated fatty acids (F_{TA}), A^n_t -oxidant vitamins, carotenoids (C^{AR}_T), Tocopherols and its versatile facets such as protein, magnesium, copper and zinc. Due to the presence of these constituents, P_{MPN} are recognized as a good reservoir for providing many health remunerations.[17]

Chemical composition of *C. pepo*

These are categorized through a low contented fat (2.3%), mono-di-poly saccharides (66%), proteinoids substances (3%) and high C^{AR}_T contented with

magnitudes of 171.9 to 461.9 microgram.[18] The mineral investigation specified that P_{MPN} pulp is enclosed with great levels of elements which shown in Table 1.[19-21] The structure of P_{MPN} S_{Ed} is reasonably varying. The content of amino acids (A^{C}_{d}), F_{TA} and minerals may differ significantly, depending on changed conditions. Such changes may be affected by differences in cultivar or origin. P_{MPN} S_{Ed} contain 50% fatty oil which is dark green and rich in free F_{TA}. The arrangement of F_{TA} differs on numerous factors(F^{CT}) like the variety of places where the P_{Lt} are developed, weather, growth F^{CT} and favoring ripeness.[22] The instabilities in the oil constituents is very high, subsequent from a wide G^{n}_{e} variation, farming atmosphere, storage time and storage conditions. The glyceride part content variates from 73.1% to 80.7 % unsaturated F_{TA}, mainly oleic acids (OA^{C}_{d}) and linoleic ($L A^{C}_{d}$). Again, the same fraction contains 19% saturated F_{TA} consisting of mainly palmitic ($P A^{C}_{d}$) and stearic acids($S A^{C}_{d}$) (6%). Several studies have reported similar types of data regarding proportions of total F_{TA} or free F_{TA} in the cake fraction of P_{MPN} S_{Ed}: 29.9% $L A^{C}_{d}$ and OA^{C}_{d} 50.4% [Table 2].

P_{MPN} S_{Ed} are enclosed comparatively huge quantities of K (5,790 µg/g dry weight) and chromium (approximately 3 µg/g dry weight), Na content of same S_{Ed} is low (6.9 µg/g dry weight). Other minerals present in P_{MPN} S_{Ed} are: P (15,700); Ca (346); iron (106); Mn (49.3); Al (9.21); Ba (1.16); Co (0.29); strontium (1.83); Ni (0.53); As (0.45) (in µg/g dry weight). Notable is the low amounts of calcium in the S_{Ed}. One hundred-gram roasted P_{MPN} S_{Ed} contain 25.94 mg Ca, 955.81 mg P and 8.06 mg of Fe.[23-25]

Numerous constituents such as C^{AR}_{T}, as lutein(L^{t}_{n}), L^{t}_{n} epoxide, 15- cis- L^{t}_{n}, 9(9') –cis- L^{t}_{n}, 13(13')- cis – L^{t}_{n}, α – C^{AR}_{T}, β- C^{AR}_{T}, violaxanthin(X^{t}_{n}), auro X^{t}_{n} epimers, flavo X^{t}_{n}, lute X^{t}_{n}, chrysanthema X^{t}_{n}, α-crypto X^{t}_{n}, β-crypto X^{t}_{n} are also present.[26-28] Acylated phenolic glycosides(G^{ly}_{o}) such as cucurbitoside F, H, I, K, L, M, 23-24- dihydro C_{CBT} lariciresinol (L^{CR}_{S}), seco-iso L^{CR}_{S}, iso L^{CR}_{S}, L^{CR}_{S} -4'-o-β-D- G^{ly}_{o}, L^{CR}_{S} - 4-o-βeta-d G^{ly}_{o}, (24s)-stigmata- 7,22E, 25-trien- 3-one, (24s)-stigmasta-7,22 E, 25 –trien-3beta-ol, C_{CBT} L 2-O-β-D-glucopyranoside.[29-31] Others Phytoconstituents are also exhibited in Table 3.

Table 1: List of minerals in P_{MPN} S_{Ed}.

Components	Nutrient value	% of RDA
Na	7 mg	0.5
K	809 mg	17
Ca	46 mg	4.5
Cu	1.343 mg	159
Fe	8.82 mg	110
Mg	592 mg	148
Mn	4.543 mg	198
P	1.233 mg	176
Se	9.4µg	17
Zn	7.81 mg	71

Anti- C_{NCR} Mechanism of *C. pepo*

C_{NCR} is the deregulation product of programmed C_{EL} death. Numerous favorable goals for mediation is recognized by reviewing the molecular defects such as the signal transduction P_{tw} that control A_{ppt}. In this viewpoint, P_{MPN} S_{Ed} comprising of C_{CBT} and its derivatives have developed a new emphasis for C_{NCR} drug discovery because of its durable ability to inhibit different types of C_{NCR}. C_{CBT} and its byproducts inhibit C_{NCR} development by a comprehensive variety of mechanisms (M_{ehs}), comprising of pro- A_{ppt}, installment of autophagy, C_{EL} cycle seizure, inhibition of C_{NCR} entrenchment and shifting. C_{CBT} also modifies numerous intracellular S_{gls} P_{tw} [Figure 3]. S_{gls} transducers and

Table 2: List of F_{TA} in P_{MPN} S_{Ed}.

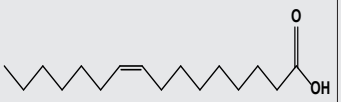
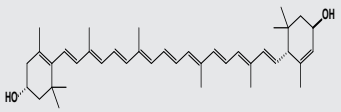
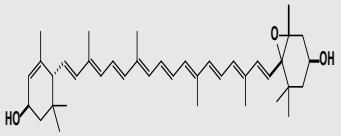
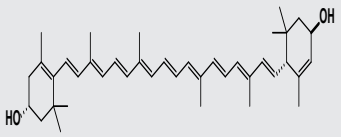
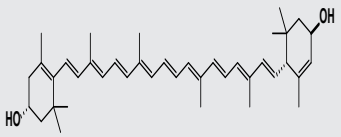
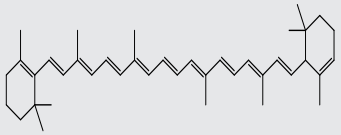
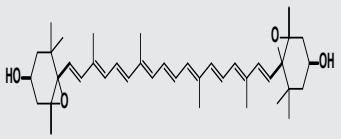
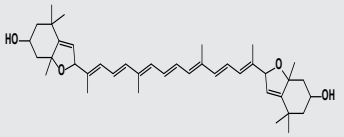
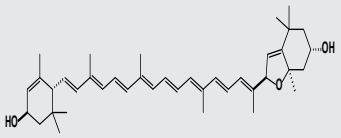
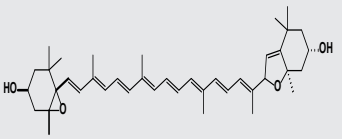
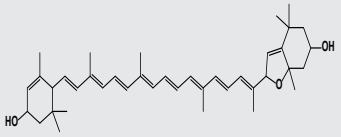
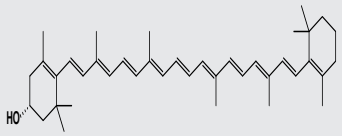
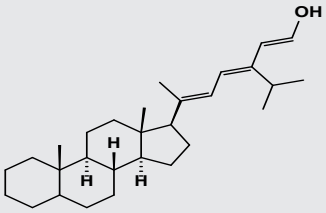
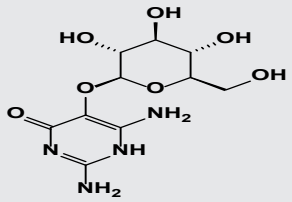
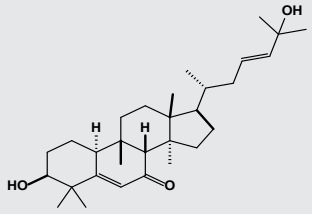
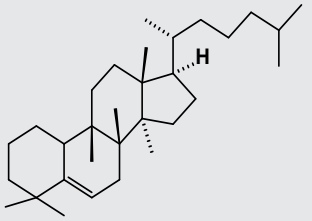
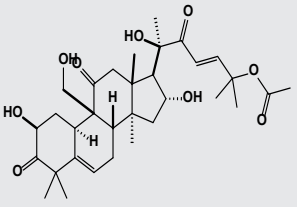
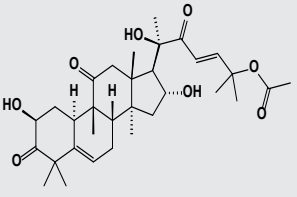
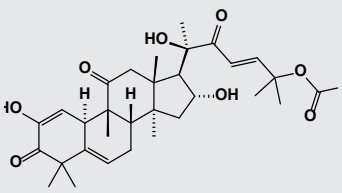
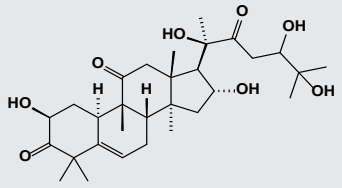
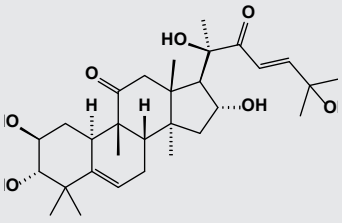
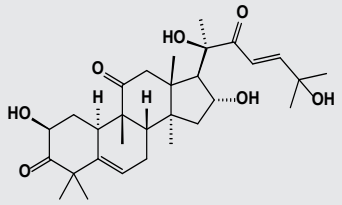
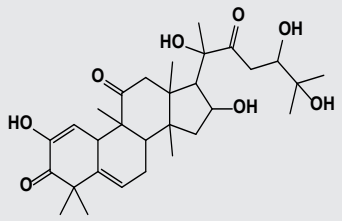
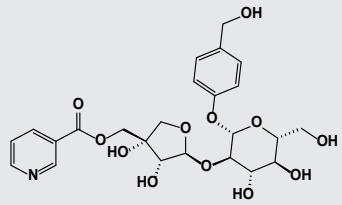
Name	Structure	Content (%)
$P A^{C}_{d}$		10.68+/-0.42
Palmitoleic A^{C}_{d}		0.58+/-0.14
$S A^{C}_{d}$		8.67+/-0.27
OA^{C}_{d}		38.42+/-0.37
$L A^{C}_{d}$		39.84+/-0.08
$L_{n} A^{C}_{d}$		0.68+/-0.14
$G_{a} A^{C}_{d}$		1.14+/-0.00

Table 3: List of Phytoconstituents present in PMPN SEd.

Name	Category	Structure
L^t_n	C^{AR}_T	
L^t_n epoxide	C^{AR}_T	
15-cis- L^t_n	C^{AR}_T	
9(9')-cis- L^t_n	C^{AR}_T	
α-carotene	C^{AR}_T	
Viola X^t_n	C^{AR}_T	
Auro X^t_n	C^{AR}_T	
Flavo X^t_n	C^{AR}_T	
Luteo X^t_n	C^{AR}_T	
Chrysanthem X^t_n	C^{AR}_T	
α-crypto X^t_n	C^{AR}_T	
Stigmastatrienol	Steroid	
Squalene	T^R_P	
Vicine	Alkaloid	
Kuguacin	T^R_P	
C_{CBT}	T^R_P	
C_{CBT} A	T^R_P	
C_{CBT} B	T^R_P	

C_{CBT} E	T^{R}_{P}	
C_{CBT} G	T^{R}_{P}	
C_{CBT} F	T^{R}_{P}	
C_{CBT} M	T^{R}_{P}	
C_{CBT} K	T^{R}_{P}	
C_{CBT} L	T^{R}_{P}	

activators of transcription (T_{R}^{SC}) 3 and Janus enzyme S_{gls} P_{tw} are the key M_{ehs} for C_{CBT} to speak into necrobiosis to place forth their compelling malignant (M^{AG}_{L}) neoplasm impact. The capability of C_{CBT} to prevail C_{EL} cycling in the G2/M part by diversified controllers is additionally a major approach to fight different C_{NCR}.[32] STAT3 (S_{ta}^{3}) controls the exposition of genes (G^{n}_{e}) which intercede multiplication (e.g., c-myc and cyclin D1), lowers activities of pro-apoptotic G^{n}_{e} (e.g., Bcl-xL, Bcl -2 and surviving) and/or accelerates maturation through vascular epithelial tissue protein (VEGF). Conversely, cytokines (C_{tK}) will inhibit the STAT-3 S_{gls}

Figure 1: Pumpkin Flowers and Fruits.

Figure 2: Germinated Pumpkin seed.

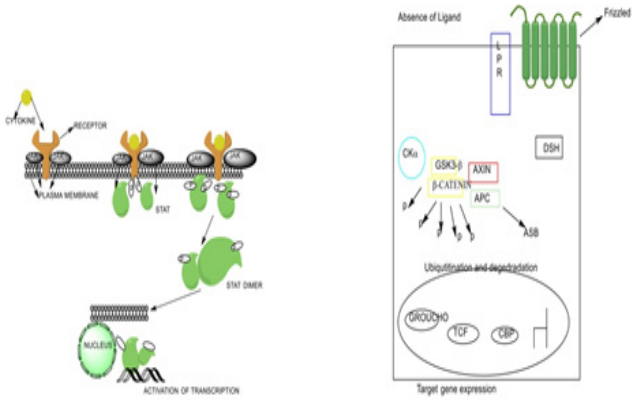


Figure 3: JAK/STAT and WNT Signaling Pathway.

P_{tw}. Protein empirical G^{n}_{e}, enacting the obliterator of C_{tK} communication super molecule family, binding to JAK, represent the major negative regulators of the JAK/ S_{ta}^{3} S_{gls} P_{tw}. In recent past, it is accepted that S_{ta}^{3} may also be called up by several alternative C_{tK}, like IL-7, IL-10, IL-20, leptin, WBC colony-stimulating issue and cuticular protein.[33] Admist the seven human STAT G^{n}_{e}, S_{ta}^{3}, a typical oncogenic communication P_{tw}, is integrally called up in many sorts of C_{NCR}, together with eighty-

two of glandular C_{Arom}, seventieth of breast (B_R^{st}) C_{NCR}, over eighty two of the C_{Arom} of the top and neck, seventy one of cavity M^{AG}_L neoplastic(N_E^{pls}) D_{SEAS}, over five hundredth respiratory organ C_{NCR} and five hundredth of HCC, lymphomas and myelomas.[34] Uncontrolled doings of S_{ta}^3 is unquestionable in an exceedingly form of t^m_R varieties, together with B_R^{st} M^{AG}_L N_E^{pls} D_{SEAS}, P_r^{st} C_{NCR}, melanoma, multiple myeloma and C_{NCR} of the blood.[35,36] Numerous G^n_e mutations cause organic activation of S_{ta}^3, as for example over-phrasing and organic triggering of cuticular protein receptor (EGFR).[37] S_{ta}^3 takes part to t^m_R growth by widening the C_{EL} cycle by warding off necrobiosis and speculating onco G^n_e like c-Myc and Bcl-X. S_{ta}^3 has lately been incontestable to enhance glandular C_{Arom} metastasis by nurturing P_r^{st} C_{NCR} C_{EL} exodus. C_{CBT} are identified as A^n_t t^m_R agents associated with other M_{ehs}, like conflicting with S_{ta}^3 S_{gls}. They also influence the virtue of the actin cytoskeleton. As for instance, C_{CBT} E wards off the propagation of glandular C_{Arom} C_{EL} and disrupts the body architecture of simple protein and supplements.[38] However, C_{CBT} A, B, E, I impede the phosphorylation (P^S_{HR}) of S_{ta}^3 and/ or JAK2 and same way rules out S_{ta}^3 deoxyribonucleic A^C_d-attachment and S_{ta}^3-mediated cistron T_R^{SC} in C_{Arom} A549 line.[39] Similiarly, C_{CBT} I causes debasement of P^S_{HR} - S_{ta}^3 in the B_R^{st}, P_r^{st} and exocrine gland M^{AG}_L N_E^{pls} D_{SEAS} C_{EL} lines (MDA-MB-231, MDA-MB-468 and Panc-1). Amazingly C_{CBT} B and E are set out to persuade P^S_{HR} of S_{ta}^3 in C_{Arom} C_{EL} lines (MDA-MB-231 and MCF-7).[40] This study indicates that C_{CBT} exerts A^n_t -tumorigenic activity by selection of C_{EL} with activated S_{ta}^3. In SAR consideration it is found that 5 C_{CBT} A, B, E, I and Q obstruct the actuation of S_{ta}^3 and produce necrobiosis. In an exceeding mouse t^m_R heterograft model, C_{CBT} however did not suppress t^m_R growth. This indicates that JAK2 inhibition isn't adequate to ward off tmR advancement suggesting thereby the power of C_{CBT} to impede t^m_R growth expounding its A^n_t - S_{ta}^3 activity. These observations more legitimize S_{ta}^3 as a drug exposition designing and supply proof that medical specialty assistants like C_{CBT} may judiciously cut back the P- S_{ta}^3 levels in human C_{NCR} C_{EL}. In distinction, K-Ras (R^a_S) mutations are found in thirty-five hundredths of primary large intestine C_{NCR} besides as in entrenched C_{Arom} C_{EL} lines. Thus, the company of oncogenic K- R^a_S considerably shrivels the sensitivity of C_{EL} to dihydro C_{CBT} B, R and I presumably through K- R^a_S disagreement with S_{ta}^3 arousal. Moreover, p53 and p21 shield C_{EL} from necrobiosis are lured by C_{CBT}. The similar studies ascertain that reactivity of human C_{Arom} C_{EL} lines to those 3 C_{CBT} falls back on the vicinity of oncogenic K- R^a_S and p53/p21 standing and establish that C_{CBT} exerts A^n_t - t^m_R genic activity within the absence of activated S_{ta}^3.[41]

Induction of A_{ppt}

C_{CBT} B, D, E, I and IIa influence A_{ppt} in different classes of C_{NCR} C_{EL} by arresting the S_{ta}^3 P_{tw}. S_{ta}^3 is a T_R^{SC} F^{CT} that rolls G^n_e expression *via* cross-talk with another T_R^{SC} F^{CT}, such as β- (B_c^n), hypoxia-inducible factor-1, nuclear factor-B, c-myc, c-jun and closing off S_{ta}^3 stimulation influenced A_{ppt}. C_{CBT} B has distinct structural ups and downs as symbol for A_{ppt}, which consists of nuclear fragmentation, chromatin contraction and embodiment of apoptotic bodies. C_{CBT} B may be significant for both inflecting the empathy of C_{NCR} C_{EL} to cytotoxic lymphocyte and inspiring A^n_t C_{NCR} immunity by the prohibition of the JAK2/ S_{ta}^3 P_{tw}. These M_{ehs} pinpoint that prohibition of the JAK/ S_{ta}^3 P_{tw} with C_{CBT} B may be impressive in C_{NCR} immunotherapy. Moreover, in human colon adeno C_{Arom}, the C_{CBT} B-influenced- A_{ppt} is sustained by a reactive oxygen species system instead of that of S_{ta}^3. C_{CBT} D stimulates the apoptotic P_{tw} by annihilating S_{ta}^3 activity in B_R^{st} C_{NCR} C_{EL} and splitting fragments to procaspase-3, procaspase -9 and PARP in human endometrial as well as ovarian C_{NCR} C_{EL}.[42-45]

Induction of Autophagy

C_{CBT}, specifically C_{CBT} B and I, activate autophagosome development. They also initiate the gathering and changing over from light chain 3-I to LC3II in several C_{EL} classes basically through inflation of production of mitochondrial-derived ROS and consequently activating ERK and JNK. Initiation is accomplished through the calling up of AMP-triggered protein kinase (K^N_s)/ mammalian target of p70S6K P_{tw} instead of PI3K/Akt P_{tw}.[46]

Induction of Cell Cycle Arrest

In human C_{EL} cycle changeover is organized by holoenzymes comprising of reciprocally regulatory and catalytic cyclin-dependent K^N_s. CDK (c^D_k) inhibitors like c^D_k 1, p21Waf1 and p27KIP1 perform as intrinsic controllers of C_{EL} cycle by hooking up to c^D_k complexes and lowering K^N_s activity.[47] C_{CBT} persuades C_{EL} cycle blockage by reshaping different S_{gls} P_{tw}. C_{CBT} B brings about G2/M C_{EL} cycle apprehend in different C_{NCR}, such as, osteosarcoma C_{EL}, non-small C_{EL} lung (L^G_u), B_R^{st} C_{NCR}, glioblastoma multiform, cutaneous squamous C_{EL}, laryngeal squamous and pancreatic C_{EL} C_{Arom}.[48-54]

Inhibition of C_{NCR} Invasion and Migration

C_{CBT} B significantly destroys C_{EL} migration and invasion induced by impeding the P^S_{HR} of Akt, p38 and ERK1/2 and the down-settlement of MMP-9. C_{CBT} E destroys

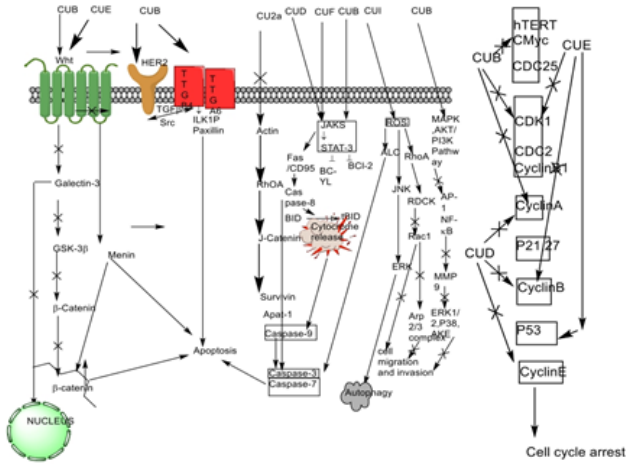


Figure 4: Mechanisms for anticancer activity of *C. pepo*. For apoptosis, Cucurbitacin B (CuB) and Cucurbitacin E (CuE) inhibit Wnt and STAT3 signaling pathways; CuB inhibits HER2 and integrin signaling pathways and elevates intracellular level of ROS; CuD inhibits STAT3 activation; Cu IIa inhibits survivin. For autophagy, CuI increases intracellular level of ROS. To inhibit cell migration and invasion, CuE and CuI inhibit Rac1 activation and Cu B inhibits phosphorylation of ERK1/2,p38 and Akt. For cell cycle arrest, CuB, CuD, CuE down-regulate protein expression of key regulators of cell cycle.

B_R^{st} C_{NCR} metastasis by distracting Arp/23-reliant actin polymerization and hindering the Src/FAK/Rac/JNK/MMP S_{gls} $P_{tw.}^{55\text{-}85}$ C_{CBT} B management restrains cyclin D1, c-Myc and B_c^n view height, alteration to the nucleus of B_c^n and galectin-3. Summarized form of A_t^n - C_{NCR} M_{ehs} is shown in Figure 4.

CONCLUSION

It may be concluded that due to phytochemical, pharmacological and nutritional values, *C. pepo* has attained high importance throughout the world. The available research data on C_{CT} indicate its M_{edc} value especially for hyperplasia, P_r^{st} C_{NCR}, urinary D_{SEAS}, nephritis, bronchitis, hemorrhoid and anemia. The M_{edc} properties of *C. pepo* are due to the presence of different phytochemicals like Triterpene (T^R_p), alkaloid, cardiac G^{ly}_o, etc. So, increasing M_{edc} value of *C. pepo* is demanding for the discovery of more potential phytochemicals which can lead to the improvement in drug formulation system. Pharmacological studies confirm the A_t^n bacterial, A_t^n viral, A_t^n ulcer and A_t^n t^m_R activities that provide scientific basis to the use of *C. pepo* based on the traditional medicines but there is no report for formulation development. Different C_{CBT} compounds are also used to inhibit uncontrolled C_{EL} division and induce A_{ppt} using plentiful C_{NCR} C_{EL} lines of human and t^m_R xenografting of leukemia, lymphoma, B_R^{st}, P_r^{st}, L_u^G, uterine cervix, liver, $^{Sk}_N$, colon, laryngeal, brain and pancreatic C_{NCR}. C_{CBT} has also the capacity to prevent P_{HR}^S of S_{ta}^3 and/or JAK2 and their consecutive invigoration play the sizable role in terms of mode of operation. C_{CBT} warrant eventual inquisitions exploring their exposition in uninvestigated origins and their offshoots for bettering the A_t^n - C_{NCR} competence. Moreover, preclinical and clinical abstraction involving united regimen including C_{CBT} and standard chemo-immune- and/or radio-therapies should be programmed for future strategies.

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CONFLICT OF INTEREST

Authors declare that there is no conflict of interest in this manuscript.

ABBREVIATIONS

A_C^d: Amino acids; **A_t^n:** Anti; **Appt:** Apoptosis; **B_R^{st}:** Breast; **C_{NCR}:** Cancer; **C_{CNG}:** Carcinogenesis; **C_{Arom}:** Carcinomas; **C^{AR}_T:** Carotenoids; **c^D_k:** CDK; **C_{EL}:** Cell; **C_{CT}:** Cucurbita; **C_{CBT}:** Cucurbitacin; **C_{tK}:** Cytokines; **D_{SEAS}:** Diseases; **F^{CT}:** Factors; **F_{TA}:** Fatty acids; **F_r^{ut}:** Fruit; **G^n_e:** Genes; **G^{ly}_o:** Glycosides; **K^N_s:** Kinase; **L^{CR}_S:** Lariciresinol; **L A^C_d:** Linoleic; **L_u^G:** Lung; **L^t_n:** Lutein; **M^{AG}_L:** Malignant; **M_{ehs}:** Mechanisms; **M_{edc}:** Medicinal; **N_E^{pls}:** Neoplastic; **OA^C_d:** Oleic acids; **P A^C_d:** Palmitic; **P_{tw}:** Pathway; **P_{Lt}:** Plant; **P_r^{st}:** Prostate; **P_{MPN}:** Pumpkin; **R^a_S:** Ras; **S_{Ed}:** Seed; **S_{gls}:** Signaling; **$^{Sk}_N$:** Skin; **S_{ta}^3:** STAT3; **S A^C_d:** Stearic acids; **T_R^{SC}:** Transcription; **T^R_P:** Triterpene; **t^m_R:** Tumor; **X^t_n:** Xanthine.

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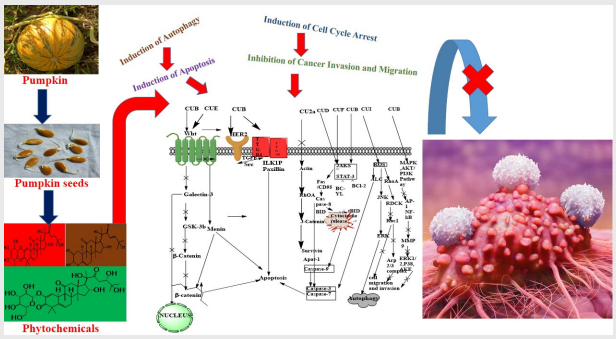
PICTORIAL ABSTRACT



SUMMARY

- Pumpkin seed contains cucurbitacin and its derivatives
- They are anti-proliferative agents
- These are blocked by JAK/STAT signaling pathway
- Blocking by JAK/STAT signaling pathway may involve several mechanisms such as induction of autophagy, induction of cell cycle arrest, induction of apoptosis, and inhibition of cancer Invasion and migration.

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