Navyug Vidyabhavan Trust's
C. K. Pithawalla Institute of Pharmaceutical Science & Research, Surat - 395007

Dedicated to

Honourable Late. Shri. Chhotubhai K. Pithawalla

(Founder & President)

Navyug Vidhyabhavan Trust, Surat

EDITOR'S MESSAGE

Prof. Dr. Mahesh. G. Saralai
Principal,
C. K. Pithawalla Institute of Pharmaceutical Science and Research, Surat.

It gives me an immense pleasure to publish with pride **CKPIPSR E-Newsletter, Volume -7 Issues I, 2016**. The pride of every student and staff would be in his/her college. It was quite inspiring to watch and witness the potential of our students/staff unfolding at various stages and situations each day. Trying and testing times during the hectic semester system have elicited our students to put forth their best. A college may reach heights of glory but without materials like a college newsletter, the outside world may not know of it. Therefore, a college bulletin is vital in promoting what an institution offers. CKPIPSR Newsletter carries the contributions reflecting ethos and aspirations of the students, faculty and other team members of the institution. CKPIPSR Newsletter brings to light the names of the unsung heroes and their mighty deeds. I am happy that there is a dedicated team of staff and students who have presented the astonishing achievements of C.K.Pians in the fields of academics, research, sports and extra-curricular activities.

The management and the staff have been supportive of the various activities that were undertaken by the students in view of helping them reach the pinnacle of perfection and professionalism in whatever task they took on thus strengthens our journey of achieving excellence. There is nothing… absolutely nothing that stops the C.K.P.I.P.S.R juggernaut from rolling forward, going on boldly from one project to another leaving the spectators spell-bound. Everything that C.K.P.I.P.S.R. touches turns into gold.

It continues to sustain its growth. People reading this newsletter will realize the tremendous changes that are happening in the C.K.P.I.P.S.R. Campus. The CKPIPSR Newsletter is presenting a glimpse of the growth of the institution on many fronts. The college has been simply unstoppable in its progress as it has been actively involved in various activities that have brought to light the hidden talents of the college students and staff. The highly qualified and dedicated members of staff have always stood shoulder with the Principal and it is always a pleasure to be a part of a team which strives to bring out the talents of students.

CKPIPSR Newsletter has recorded achievements such as: academic excellences,conferences attended by staff members and students, competitions won by the hugely talented students/Staff, innovative projects carried out by students with the guidance of staff, among others. They stand as a witness to the monumental efforts taken by the management to make the college a centre of excellence in education and research.

I am sure the college will scale even greater heights in the years to come and serve many more millions in the society.

Congratulations to **Ms.Shivali Desai, Assistant Professor, Department of Pharmaceutical Chemistry and Co-ordinator/Co-editor of CKPIPSR Newsletter** and my team for their determined efforts in bringing out this Newsletter.

CO-EDITOR'S MESSAGE

Ms. Shivali B. Desai,
Assistant Professor (Department of Pharmaceutical Chemistry)
C. K. Pithawalla Institute of Pharmaceutical Science and Research, Surat.

It is a great privilege for me to handover the **C.K.P.I.P.S.R. E-Newsletter, Volume -7, Issues I, 2016** of C.K.Pithawala Institute of Pharmaceutical Science and Research, Surat.

This E-Newsletter not only encompass the academic achievements of C.K.P.I.P.S.R. family but it also gives a vigorous picture of our student's caliber in painting, poetry, stories, literature and their enthusiasm in sports and cultural activity.

Being a co-ordinator of e-newsletter requires a lot of hard work and presence of mind but it has made my job easier knowing that I have a reliable guide, the Principal Sir and supportive staff. I express my sincere gratitude to our Respected Principal, **Prof. Dr. Mahesh G. Saralai** for giving me an opportunity to build this e-newsletter. I also thank my colleagues, students and social well wishers for their co-operation, support and encouragement during compilation of this e-newsletter.

I also take this opportunity to accept healthy criticism or suggestion for better edition of **CKPIPSR E-Newsletter** in the future.

A GESTURE TO PROFESSION

BISHNUPADA MUKERJEE

A Medico-Pharmaceutical Professional of Eminence

Bishnupada Mukerjee was an Indian pharmacologist, known for his contributions in the fields of pharmacological research and standardization of drugs in India. The Government of India honoured him in 1962, with the award of Padma Shri.

Date of Birth: 1st March, 1903

Place of Birth: Barrackpore, West Bengal, India

Occupation: Pharmacologist

Educational Track:

School: Barrackpore (West Bengal)

College: Scottish Church College, Kolkata

Higher Study: Culcutta Medical College

WORK EXPERIENCE

1927-28: worked as Resident House Surgeon at the Eden Hospital of the College.

1930: become an assistant secretary at the Drugs Enquiry Commission.

1931-1933: worked at the culcutt school of Tropical Medicine.

1933: went abroad as Rockefelller Foundation Fellow and worked in different counties till January,1937.

1933: reported that an alkaloid obtained from the plant, on experimental studies in animals showed central depressant properties and lowered the blood pressure.

1937: he returned to India to be reunited with Ram Nath Chopra at the All India Institute of Hygiene and public Health.

1941: became director of the institution at Kolkata and late at kasauli.

1945: became the first member of Advisory Board of the Indian Pharmacist Journal.

1947: he was appointed as the director of Central Drug Laboratory.

1948: came with the plan to establish a national laboratory to be called 'Central Drug Research Institute (CDRI)'

1951: Dr B. Mukerji became the first permanenat director of the institute where he worked till 1963.

1946-1952: he was the general secretary of the Indian Science Association.

1963: became director of Chittaranjan National Cancer research Centre, Kolkata upto his retirement in 1968.

1966: he was the chairman of the committee which published the second edition of Indian Pharmacopoeia.

AWARDS AND HONOURS

1938: The Griffith Memorial Prize and The Nilmony Brahmachari Gold Medal of the University of Kolkata.

1940: The Asutosh Mookerjee Memorial Award of the Indian Science Congress Association.

1951: The Indian Science Congress Medal

1954: The Barclay Medal of the Asiatic Society.

1962: The Squibb International Award

1963: H. K. Sen Memorial Medal

1976: Acharya P. C. Ray Medal and Shree Dhanwantari Medal

1962: The award of Padma Shri.

Bishnupada Mukerjee died on 30th July 1979.

ACADEMIC EXCELLENCE

WINTER-2015 EXAM

- **Seventh Semester** – **Three** students secured more than 8 SPI while **nine** students secured more than 7 SPI in Winter-2015 exam.
- **Fifth Semester** – **Two** students secured more than 8 SPI while **five** students secured more than 7 SPI in Winter-2015 exam.
- **Third Semester** – **Three** students secured more than 8 SPI and **fourteen** students secured more than 7 SPI in Winter-2015 exam.
- **First Semester** – **Two** students secured more than 8 SPI while **sixteen** students secured more than 7 SPI in Winter-2015 exam.

Meritorious Students

Class	Rank	Name of Student	SPI
Semester-VII	1	Motwani Avinash	8.73
	2	Shah Mansi	8.09
	3	Patel Henisha	8.00
Semester-V	1	Qadri Misbah S.	8.36
	2	Shaikh Zebabibi Z.	8.00
	3	Gajjar Hiral	7.55
Semester-III	1	Patel Bansari Bharatbhai	8.45
	2	Jangid Jyoti Harishbahi	8.36
	3	Patel VyomaTejasbhai	8.27
Semester-I	1	Singh Chandani K.	8.15
	2	Hakeem Safiya A.	8.12
	3	Lehankar Swapnil S.	7.91

GPAT QUALIFIERS

Academic Year 2015-16

Sr.No.	Name of Student	GPAT Score	All India Rank
1	Singh Ankita	123	1489
2	Shah Mansi	118	1881
3	Gamit Sheron	99	4393

Statewise ranking of the Institute at GTU, Gandhinagar (2015-16)

Semester	% of Result of Institute	Institute wise rank
7th	71.43%	3
5th	40.00 %	27
3rd	55.56%	12
1st	37.70 %	12

FEATHERS ON THE CROWN

Conference/Seminar/Workshop attended by Faculty

- ✓ Ms.Richa Champaneria attended GUJCOST sponsored seminar on **"Academia-Industry Interaction: Hopes and Promises"** at K.B.Institute of Pharmaceutical Education and research, Gandhinagar on 30thJanuary, 2016.
- ✓ Mrs.Prakruti Jadav, Ms.Shivali Desai, Ms.Richa Champaneria, Mrs.Mitali Patel and Ms.Bhavi Patel attended the Southern Gujarat Chamber of Commerce organized workshop on **"How to get your Innovation Patented"** at Samruddhi Hall, Nanpura, Surat on 4th Feb, 2016.
- ✓ Dr. M.G.Saralai (Resource Person, Chairman) and Dr. Pinal Harde (Delegate) and Mrs.Prakruti Jadav (Delegate) attended GUJCOST sponsored national conference on **"Emerging trends in Pharmaceutical Science and Regulatory Affairs"** at Bhagvan Mahavir College of Pharmacy, Surat on 6th February, 2016.
- ✓ Ms. Shivali Desai, Ms.Richa Champaneria, Mrs.Pratixa Patel, Mrs.Arti Patel and Mr. Smit Patel attended GUJCOST sponsored one day symposium on **"Innovations and Practices in Teaching Learning Pedagogy"** at Maliba Pharmacy College, Tarsadi on 26th March, 2016.
- ✓ Ms.Richa Vasava attended GTU organized **"Soft Skill Development Programme"** at Shree Nanjibhai Lalbhai Patel College of Pharmacy, Umrakh on 30th March, 2016.
- ✓ Dr. M.G.Saralai (Resource Person, Chairman) and Dr. Ashok Akabari (Judge) attended GUJCOST sponsored 4th International Conference on **"Theranostic Nanoparticles: A recent Breakthrough in Nanotechnology"** at Shree Dhanvantary Pharmacy College, Kim on 15th & 16th April, 2016.
- ✓ Ms.Richa Champaneria, Mr. Vishal Patil and Mr. Manoj Alai attended and presented poster at GUJCOST sponsored 4th International Conference on **"Theranostic Nanoparticles: A recent Breakthrough in Nanotechnology"** held at Shree Dhanvantary Pharmacy College, Kim on 15th & 16th April, 2016. Mr.Vishal Patil secured 2nd Prize in Poster Presentation.

Conference/Seminar/Workshop attended by Students & achievements

- ✓ Thirty one students from eighth and sixth semester attended GUJCOST sponsored one day national seminar on **"Futuristic Perspective on Inhaled Drug Therapy"** organized by Maliba Pharmacy College, Tarsadi on 9th January, 2016.

- ✓ Thirteen students from fourth semester participated in various competitions like Poster Presentation, Recycle, Snapster, Antakshari, Pharmaword, Mock Interview, Powerpoint Presentation, Drug Connect, Pharma Race and Case Study at **"ENIGMA 2016"** organized by Nirma University, Ahmedabad on 1st and 2nd February, 2016. Students got:
  Ist Prize (Recycle): Patel Bhavya, Patel Divya
  Ist Prize (Snapster): Rangwala Yasmin
  IInd Prize (Poster Presentation): Motwani Kunal, Shaikh Quaratulain

- ✓ Twenty five students from eighth and sixth semester attended and presented posters at GUJCOST sponsored national conference on **"Emerging Trends in Pharmaceutical Sciences and Regulatory Affairs"** held at Bhagavan Mahavir College of Pharmacy, Surat on 6th February, 2016.

- ✓ Nineteen students from fourth semester participated in various competition namely Dare to Do, Scitoon, Youth Conclave, Quize Competition, Pharma Dumb Charades, Model and Poster Presentation **"AVALANCHE'16"** organized by Rambhai Patel College of Pharmacy, Changa on 18th & 19th February, 2016. Students got:
  Ist Prize (Poster Presentation): Bamania Prem, Patel Vrushti, Thakkar Hiren
  Ist Prize (Scitoon): Patel Shradhdha, Baria Niketa

- ✓ Thirty students from sixth and fourth semester participated in competitions namely Pharma Recipe, Myself Medicine and Model Presentation at **"GTU Techfest 2016"** held at Swami Atmanand Saraswati Institute of technology, Surat on 26th and 27th Feb, 2016. Students got:
  IInd Prize (Pharma Recipe): Shaikh Zeba, Indave Jaya, Patel Jignasa, Patel Foram
  IInd Prize (Model Presentation): Patel Bansari, Patel Vyoma, Rangwala Yasmin, Lohia Naman, Baria Niketa

- ✓ Seven students from fourth semester participated in **"PHARMANTHAN'16"** organised by B.K.Modi Gov.Pharmacy College, Rajkot on 16th and 17th March, 2016. Students got:
  IInd Prize (Poster Presentation): Bamania Prem
  IIIrd Prize (Pharmaskit): Tiwari Ankit, Sonagara Payal, Vanecha Swati

- ✓ Fifteen students from second and fourth semester participated in competition like Poster Presentation, Rangoli Competition, Bike Race, Drawing Competition at **"SPRINGFEST'16"** organized by Mahavir Swami College of Engineering, Surat on 21st and 22nd March, 2016

- ✓ Twenty three students from fourth and second semester attended GUJCOST sponsored 4th International Conference on **"Theranostic Nanoparticles: A recent Breakthrough in Nanotechnology"** at Shree Dhanvantary Pharmacy College, Kim on 15th & 16th April, 2016. Students also participated in Poster Presentation, Solo Dance Competition, Singing Competition and got:
  IInd Prize (Poster Presentation): Mishra Dhiraj K., Patel Jay A.

PUBLICATION

- ✓ A review on **"Endophytic Fungi from Musa Paradisiaca as Anti-diabetic agent"** by M. G. Saralai, Nirav Gheewala*, Hasumati A. Raj, Gautam Sonara, Rajat Bucha and Ridhdhesh Jivawala; Annals of Pharma Research, 2015, 4(01), 205-208.
- ✓ A research on **"Development and Validation of Stability Indicating RP-HPLC Method for Estimation of Fluvastatin Sodium in Bulk and Capsule Dosage Form"** by Ashok Akabari*, Bhanubhai Suhagia, Mahesh Saralai, Vishnu Sutariya; Eurasian Journal of Analytical Chemistry-00016-2016-02.
- ✓ A review on **"Herbal's use for Parkinson and Various Procedures for Parkinson Disease"** by M.G.Saralai, Patil Vishal S.* and Manoj Alai; Journal of Bioinnovation, 2016, Volume 5, Issue 4.
- ✓ A review on **"Leptin Signaling and Development of Hypertension in Obesity"** by P. K. Jadav*, M.G.Saralai, A.G.Gandhi, B.M.Patel; Inventi Rapid:Molecular Pharmacology, 2016(2):1-5, 2016.

UPCOMING EVENTS

- ✓ GSPC sponsored **First Refresher Course for Registered Pharmacist** on **30th-31st July, 2016** at **C.K.Pithawalla Institute of Pharmaceutical science & Research**, Dumas road, Surat.
- ✓ GSPC sponsored **Second Refresher Course for Registered Pharmacist** on **17th-18th September, 2016** at **C.K.Pithawalla Institute of Pharmaceutical science & Research**, Dumas road, Surat.
- ✓ 7th international conference on **Stem Cells & Cancer (ICSCC-2016): Proliferation, Differentiation and Apopstosis** on 21st-23rd October, 2016 at Goa.
- ✓ World Congress on **Drug Discovery & Development** on 23rd-25th November, 2016 at Bangalore.
- ✓ **68th Indian Pharmaceutical Congress** on 16th-18th December, 2016 held at Andhra University, Visakhapatnam, Andhra Pradesh.

GUEST LECTURES ORGANISED

- ✓ A guest lecture on a topic of **"Swadeshi Chikitsha-based on home remedies"** by Dr.Arun Mishra and Mr.Kirti Patel, Surat, was oraganised on 8th March, 2016.
- ✓ A guest lecture on a topic of **"Breast Cancer Awareness"** by Dr.Shweta Vyas Bhagat, Florence Hospital, Surat, was oraganised on 9th March, 2016.

- ✓ A guest lecture on a topic of **"MBA in Pharma Marketing and in International Business Management"** by Dr.Pradip Manjrekar and Mr.A.Vivek, D.Y.Patil University, Mumbai, was organized on 17th March, 2016.

EVENTS ORGANISED

Free Health Check-up Camp & Blood Donation Camp on 01st March, 2016

On account of tribute to Late Shri Chhotubhai K. Pithawalla (Honorable Founder and President of Navyug Vidyabhavan Trust) on his first death anniversary, institute has organized free health checkup and blood donation camp on 1st March, 2016 at Maniben Pithawalla Nidan Kendra, Sultanabad, Surat. Total 16 doctors with specialization of Medicine, Gyneocology, opthamology, Pediatric of surat city had examined about 435 Patients. The patients and villagers are also educated about cancer awareness, its risk factors, precautions and its medication in association with "Bharat cancer Research Institute and Hospital. Blood donation camp was organized with kind support of Surat Raktdan Kendra in which about 45 units of blood was collected from volunteers.

International Women's Day on 8th & 9th March, 2016

In a View to International women's day, on 8th March 2016 women's development committee members organized quiz competition and elocution competition especially for girls students to check their knowledge by keeping one section related to women in quiz. Also a guest lecture on "was organized next day on 9th March, 2016 to celebrate the same.

Annual cum Farewell Day Celebration on 2nd April, 2016

EXCELLENCE PRESSNOTE

ફાર્મા રેસીપી અને મોડેલ પ્રેઝન્ટેશનની રજૂઆત કરાઇ

સિટી રિપોર્ટર @srt_cb

નવયુગ વિદ્યાભવન ટ્રસ્ટ સંચાલીત સી.કે.પીઠાવાલા ઈન્સ્ટિટ્યુટ ઓફ ટેકનોલોજી વિભાગનાં વિદ્યાર્થીઓએ ગુજરાત ટેકનોલોજી યુનિવર્સિટી દ્વારા 'જીટીયુ ટેકફેસ્ટ'નું આયોજન કરવામાં આવી હતી. જેમાં ફાર્મા રેસીપી અને મોડેલ પ્રેઝન્ટેશન સ્પર્ધા પણ યોજવામાં આવી હતી. જેમાં બંસરી પટેલ, નિકેતા બારીયા, નમન લોહીયા, યાસ્મીન રંગવાલા અને વ્યોમા પટેલે મોડેલ પ્રેઝન્ટેશનમાં અને શેખ ઝેબા, જયા ઈન્દવે, ફોરમ પટેલ, જિજ્ઞાસા પટેલે ફાર્મા રેસીપી સ્પર્ધામાં દ્વિતિય ક્રમાંક મેળવ્યો હતો. જીટીયુ ટેકફેસ્ટમાં વિજેતા થયેલા આ તમામ વિદ્યાર્થીઓને હાર્દિક અભિનંદન પાઠવવામાં આવ્યાં હતાં. ટેકફેસ્ટમાં સુરત તેમજ ગુજરાતની વિવિધ કોલેજોએ ભાગ લીધો હતો.

DIVYABHASKAR
05th MARCH 2016

C.K.Pithawalla Institute of Pharmaceutical Science and Research, Surat, Gujarat

C.K. Pithawalla Institute of Pharmaceutical Science and Research, Surat, Gujarat organised "Thalassemia awareness and Prevention Programme" in association with Indian Red Cross Society on 7th October, 2015. The session was started with inaugral function by dignitaries, Chief Guest Dr. Mukeshbhai Jagiwala - Secretary Indian Red Cross society, Surat and Head of the Institute Dr. Prof. Mahesh G. Saralaya. A lecture on "What is Thalassemia?", "How to prevent it?", "How screening is carried out?", was given by Dr. Mukesh Jagiwala. Later, Prof. Dr. Mahesh G. Saralaya addressed on pathophysiology of thalassemia, its relation to gene and measures to eradicate thalassemia. C.K. Pithawalla Institute of Pharmaceutical Science and Research, Surat had arranged a Campus Placement drive by Eris Lifesciences Pvt. Ltd. Ahmedabad on 10th September, 2015 and Novo Nordisk India Pvt. Ltd. Bangalore on 16th September, 2015.

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નિઃશુલ્ક આરોગ્ય તપાસ શિબિર યોજાઈ

છોટુભાઈ કે. પીઠાવાલાની પ્રથમ પુણ્યતિથિ નિમિત્તે નવયુગ વિદ્યાભવન ટ્રસ્ટ સંચાલિત સી. કે. પીઠાવાલા ઈન્સ્ટીટ્યુટ ઓફ ફાર્માસ્યુટીકલ સાયન્સ એન્ડ રીસર્ચ, દ્વારા એક દિવસીય નિઃશુલ્ક તપાસ શિબિર તથા રક્તદાન શિબિરનું મફીબેન પીઠાવાલા નિદાન કેન્દ્ર સુલતાનાબાદમાં સવારે ૯ થી ૪ દરમ્યાન આયોજન કરવામાં આવ્યું હતું. જેમાં ૪૩૫ થી વધારે લોકોએ શિબિરનો લાભ લીધો હતો.

GUJARAT SAMACHAR
09th MARCH 2016

છોટુભાઇ કે. પીઠાવાલાની પ્રથમ પુણ્યતિથિ નિમિત્તે નિઃશુલ્ક આરોગ્ય તપાસ શિબિરનું આયોજન

નવયુગ વિદ્યાભવન ટ્રસ્ટના સંસ્થાપક છોટુભાઈ કે. પીઠાવાલાની પ્રથમ પુણ્યતિથિ નિમિત્તે નવયુગ વિદ્યાભવન ટ્રસ્ટ સંચાલિત સી. કે. પીઠાવાલા ઈન્સ્ટીટ્યુટ ઓફ ફાર્માસ્યુટિકલ સાયન્સ એન્ડ રીસર્ચ, સુરત દ્વારા એક દિવસીય નિઃશુલ્ક તપાસ શિબિર તથા રક્તદાન શિબિરનું મફીબેન પીઠાવાલા નિદાન કેન્દ્ર સુલતાનાબાદમાં આયોજન કરવામાં આવ્યું હતું. જેમાં ૪૩૫થી વધારે લોકોએ લાભ લીધો. શિબિરમાં મહેરના જાણીતા તબીબો ડો. ચેતા ભગત, ડો. નિલેશ પટેલ, ડો. અભિજિત મોદી, ડો. હીરેન શાહ, ડો. નિકીશ ભગત, ડો. સંગીતા કેશમુખ, ડો. મુકેશ જગીવાળા, ડો. સમીર શાહ તથા ડો. જીતેન્દ્ર પટેલ, ડો. મનુભાઈ પટેલ, ડો. સી. પી. કટવાર, ડો. ઉદેશી મરકાવાલા, ડો. મનિષ શિલ્પ, ડો. જે. એચ. પટેલે સેવાઓ આપી હતી. આ શિબિરમાં વિના મૂલ્યે દવાઓનું વિતરણ કરવામાં આવ્યું હતું. રક્તદાન શિબિરમાં ૫૦થી વધુ લોકોએ રક્તદાન કર્યું હતું.

સંસ્થાના ટ્રસ્ટી મણેશભાઈ પીઠાવાલા, રમેશભાઈ મિસ્ત્રી, દક્ષિણ ગુજરાત યુનિવર્સિટીના કુલપતિશ્રી દક્ષેશભાઈ ઠાકર તથા આચાર્ય ડો. મહેશ જી. સરલાય તથા સી. કે. પીઠાવાલા એન્જીનીયરીંગ કોલેજના આચાર્ય ડો. અનિષ ગાંધી ઉપસ્થિત રહ્યા હતા. મણેશભાઈએ પિતાના માનમાં દર વર્ષે પુણ્યતિથિ નિમિત્તે શિબિરનું આયોજન કરવાનો નિર્ણય જાહેર કર્યો છે.

GUJARAT MITRA
2ND MARCH, 2016

DIVYABHASKAR
03rd MARCH 2016

સાર સમાચાર

C. K. પીઠાવાલા પુણ્યતિથિએ મેડિકલ કેમ્પ

સુરત। નવયુગ વિદ્યાભવન ટ્રસ્ટ સંચાલિત સી.કે.પીઠાવાલા ઈન્સ્ટિટ્યુટ ઓફ ફાર્માસ્યુટિકલ સાયન્સ એન્ડ રિસર્ચ દ્વારા સ્વ.છોટુભાઈ પીઠાવાલાની પ્રથમ પુણ્યતિથિ નિમિત્તે તા.1 માર્ચે નિઃશુલ્ક તપાસ શિબિર તથા રક્તદાન શિબિરનું આયોજન કરવામાં આવ્યું હતું. જેના 435થી વધારે લોકોએ શિબિરનો લાભ લીધો હતો.

સી. કે. પીઠાવાલા ફાર્માસ્યુટીકલ સાયન્સ એન્ડ રીસર્ચ, સુરતનું ગૌરવ

GUJARAT MITRA
07th FEBRUARY 2016

ફાર્મામંથનમાં પીઠાવાલા ટીમે ભાગ લીધો

સિટી રિપોર્ટર @srt_cb

બી.કે.મોદી ગર્વમેન્ટ ફાર્મસી કોલેજ દ્વારા ફાર્મામંથન-16નું આયોજન કરવામાં આવ્યું હતું, જેમાં સી.કે.પીઠાવાલા ઈન્સ્ટિટ્યુટ ઓફ ફાર્માસ્યુટીકલ સાયન્સ એન્ડ રીચર્સનાં પ્રેમ બામણીયાએ બીજો, ફાર્માસ્કીટ સ્પર્ધામાં સ્વાતિ વાણેચા, પાયલ સોનાગરા અને અંકીત તિવારીએ ત્રીજો ક્રમ મેળવ્યો હતો. આ તમામ વિદ્યાર્થીઓને અભિનંદન આપવામાં આવ્યા હતાં.

DIVYABHASKAR
26th MARCH, 2016

સી.કે.પીઠાવાલાની ટીમ એનીગ્મામાં વિજેતા થઇ

સિટી રિપોર્ટર @srt_cb

નિરમા ઈન્સ્ટિટ્યુટ ઓફ ફાર્મસી સ્ટુડન્ટ એસોસિએશન દ્વારા એનીગ્મા-2016નું આયોજન કરવામાં આવ્યું હતું. આ સ્પર્ધામાં સી.કે.પીઠાવાલા ઈન્સ્ટિટ્યુટ ઓફ ફાર્માસ્યુટીકલ સાયન્સ એન્ડ રીસર્ચના સેકન્ડ યરના સ્ટુડન્ટસ ભવ્ય પટેલ, દિવ્યા પટેલ અને યાસ્મી રંગવાલાએ સ્નેપસ્ટરમાં પ્રથમ ક્રમ મેળવ્યો હતો તેમજ પોસ્ટર પ્રેઝન્ટેશનમાં કુણાલ અને કુરાતુલૈને બીજો ક્રમ મેળવ્યો હતો.

DIVYABHASKAR
07th FEBRUARY 2016

પીઠાવાલામાં ટેક ફેસ્ટ

સી. કે. પીઠાવાલા ઈન્સ્ટિટ્યુટ ઓફ ફાર્માસ્યુટિકલ સાયન્સ એન્ડ રિસર્ચ સુરતના વિદ્યાર્થીઓએ ટેકનોલોજિકલ યુનિવર્સિટી દ્વારા આયોજીત જીટીયુ ટેકફેસ્ટ-૨૦૧૬માં ઉજ્જવળ દેખાવ કર્યો હતો. બંસરી પટેલ, નિકેતા બારિયા, નમન લોહીયા, યાસ્મીન રંગવાલા, વ્યોમા પટેલએ પ્રેઝન્ટેશનમાં તથા ઝેબા શેખ, જયા ઈન્દવે, ફોરમ પટેલ, જિજ્ઞાસાએ ફાર્મા રેસીપી સ્પર્ધામાં દ્વિતિય ક્રમાંક મેળવ્યો હતો.

SANDESH
05th MARCH, 2016

સી. કે. પીઠાવાલા ફાર્માસ્યુટીકલનું ગૌરવ

નવયુગ વિદ્યાભવન ટ્રસ્ટ સંચાલિત સી.કે. પીઠાવાલા ઈન્સ્ટીટ્યુટ ઓફ ફાર્માસ્યુટીકલ સાયન્સએન્ડરીસર્ચ, સુરતના સેકન્ડ યર બી.ફાર્મના વિદ્યાર્થીઓએ તા. ૧૬.૦૩.૨૦૧૬ અને ૧૭.૦૩.૨૦૧૬ના રોજ બી.કે. મોદી ગવર્મેન્ટ ફાર્મસી કોલેજ, રાજકોટ દ્વારા આયોજીત પ્રતિસ્પર્ધી ફાર્મન્થન-૧૬માં ભાગ લીધો હતો. જેમાં પોસ્ટર પ્રેઝન્ટેશનમાં પ્રમક્ષીયા પ્રેમે દ્વિતીય ક્રમાંક મેળવ્યો હતો તથા ફાર્મસ્કીટસ્પર્ધામાં વાણેચા સ્વાતિ, સોનાગરા પાયલ અને તિવારી અંકિતે તૃતિય ક્રમાંક મેળવ્યો હતો.

GUJARAT SAMACHAR
29th MARCH 2016

SCIENTIFIC ARTICLES

Infertility and Use of Sunscreen

Prof. Dr. M .G. Saralai, Ms. Richa. I. Champaneria, Mrs. Mitali. M. Patel

Fertility rates have fallen worldwide over the last 50 years and chemicals found in everyday products are thought to be playing a role -- including those in your sunscreen.

Researchers at the University of Copenhagen found that filters commonly used in sunscreens to absorb ultraviolet light could affect male fertility by stopping sperm from functioning properly.

Niels Skakkebaek, an endocrinologist at the university's Rigshospitalet hospital unit Denmark who led the study, reported that these filters are one of a range of chemicals used in consumer products, known as endocrine disruptors that are associated with health effects such as infertility.

The researchers tested 29 of the 31 UV filters approved for use in the United States and Europe by dissolving and applying them to sperm samples provided by healthy volunteers. Almost half of the filters tested were found to stop sperm from functioning properly. These results are of concern and might explain in part why unexplained infertility is so prevalent. The team's previous research discovered that a range of endocrine disruptors could impact the functionality of human sperm. UV filters, which were found to be easily absorbed through the skin, were among them. When sunscreen is applied on the skin, some of the UV filters can penetrate the skin and go into the bloodstream and UV filters were found in more than 95% of urine samples tested as part of trials in the United States, Spain, France and Denmark.

These filters were found to affect human sperm by mimicking the effects of the female hormone progesterone. This mimicry then altered signaling inside of the sperm cells. Progesterone plays a vital role in a sperm's ability to mature and fertilize a female egg. It controls the attraction of a sperm cell toward a female egg, as well as the sperm's ability to move and break through barriers to reach the egg. When progesterone binds to a sperm cell, this leads to calcium signals being sent within the sperm, caused by changes in the concentration of calcium ions. By mimicking this effect, chemicals like the UV filters disrupt this process and change the inner workings of the sperm.

At low quantities, the UV filters were found to have an additive effect, meaning that despite being present at lower levels, they still had an impact on sperm samples when different filters were combined together. Many other environmental and lifestyle factors are also thought to be affecting the decline in sperm quality worldwide. These include smoking -- particularly exposure while in the womb -- marijuana, excessive alcohol and obesity, in addition to certain chemicals in everyday consumer products. The environment factor has a key role to play in the decline seen in fertility worldwide. More, research is needed on the effects of sunscreen on sperm, to provide the evidence.

DIURETIC STUDIES ON THE LEAVES OF SHOREA RUBASTA

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Abstract

Shorea Robusta belonging to famiy Dipterocarpaceae) ,which was of special interest to us and have commenced diligent investigation within collaboration of all ,the connected disciplines like pharmacognosy and pharmacology .The acetone and methanolic extracts of the leaves of shorea robusta screened for gross behavioral studies. The pharmacological activity was performed using albino rats. They were divided in to 4 groups having 4 animals each.Group I, administered with acetone extract of shorea robusta leaves in a dose of 100 mg/kg and group II was administered with Methanolic extract of shorea robusta leaves in a dose of 100mg/kg. Solvent control as group III, administered with 0.5 % Carboxy methyl cellulose solution. The result was seen that methanolic extract of the leaves of the shorea robusta was found to posses significant diuretic activity than compare to the acetone extract of the leaves shorea robusta and positive control..

Key words: Shorea Robusta, 0.5 % Carboxy methyl cellulose, diligent, diuretic

Secured 2nd prize GUJCOST sponsored 4th international Conference on "Theranostic Nanoparticles: A recent Breakthrough in Nanotechnology"at Shree Dhanvantary Pharmacy College, Kim (15th and 16th April 2016)

Theranostic Cubosomal Nanoparticles of Ibuprofen for Opthalmic Delivery

M. H. Alai*, M. G. Saralai, V. S. Patil
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Abstract

Over the past few years large number of new delivery systems was developed, and every system has some disadvantages over the others. Besides that; Cubosome is one of the safest delivery of drug with assumptions of Targeting and Controlling of Drugs in the humans; just because of both the type i.e. Hydrophillic as well as hydrophobic drugs can be filled. Particle size of prepared batches was found to be 190 nm with 96-97% entrapment efficiency, and zeta potential was observed with value of -17 to -24 mv, whereas p-type of Cubosomes was determined by using cryo-transmission electron microscopy (cryo-TEM). However, the release IB from Cubosomes exhibited much slower rate i.e. 90% & 80% in 24 hrs respectively from F1 & F2 formulations. Ocular irritation test indicated that score for each group was 2; and hence no any irritation to the eye. This cubosomal delivery of Ibuprofen was effective for the treatment of ocular infections and post operative inflammation as well as pain.

ANTI-PSORIATIC ACTIVITY OF *SMILAX CHINA* LINN. RHIZOME USING THE RAT ULTRAVIOLET B-RAY PHOTODERMATITIS MODEL

DHIRAJ MISHRA*, JAY PATEL (4th Semester B.Pharm), Dr. MAHESH G. SARALAI

Abstract

The plant ***Smilax china* Linn. Rhizome**, traditionally, is claimed to be useful in the treatment of psoriasis and other skin diseases. In order to evaluate this information, antipsoriaticactivity of the ethyl acetate fraction of ***Smilax china* Linn. Rhizome** at dose of 100 and 200 mg/kg were investigated using UV-B induced photodermatitis model. In the UV induced photodermatitis model, histopathological analysis of the section revealed the absence of Munro's microabscess, elongation of rete ridges and capillary loop dilation in ethyl acetate fraction (200 mg/kg) and standard group. The ethyl acetate fraction of *Smilax china* rhizome (200 mg/kg) showed maximum antipsoriatic activity (increased orthokeratotic region by 29%) when compared with a positive control. The phytochemical studies showed the presence of flavonoids in the ethyl acetate extract. We concluded, using animal model that the ethyl acetate fraction of ***Smilax china* Linn. Rhizome** has significant antipsoriatic activity.

Secured 2nd prize GUJCOST sponsored 4th international Conference on "Theranostic Nanoparticles: A recent Breakthrough in Nanotechnology"at Shree Dhanvantary Pharmacy College, Kim (15th and 16th April 2016)

DEVELOPMENT AND VALIDATION OF HPTLC METHOD FOR SIMULTANEOUS ESTIMATION OF DROTAVERINE HYDROCHLORIDE AND MEFENAMIC ACID IN THEIR COMBINED PHARMACEUTICAL DOSAGE FORM.

Jyoti Jangid*, Yasmin Rangwala, Richa Champaneria, Dr M.G.Saralai.

Abstract

A simple and sensitive high-performance thin layer chromatographic method was developed and validated for simultaneous estimation of Drotaverine Hydrochloride and Mefenamic Acid. Drotaverine Hydrochloride and Mefenamic Acid were spotted on silica gel $60F_{254}$ TLC plates, developed using toluene: methanol: glacial acetic acid (8:2:0.2, v/v/v) as mobile phase and scanned at 305 nm using a Camag TLC Scanner IV. The R_f value of Drotaverine Hydrochloride (DRO) and Mefenamic Acid (MEF) were found to be 0.35 ± 0.02 and 0.69 ± 0.02 respectively. Drotaverine Hydrochloride and Mefenamic Acid were found to be linear in the concentration range of 300 – 700 ng/band and 900 – 2100 ng/band respectively. The limit of detection and limit of quantitation for Drotaverine Hydrochloride were found to be 70 ng/band and 300 ng/band respectively and for Mefenamic Acid, 210 ng/band and 900 ng/band respectively. The proposed method was successfully applied for simultaneous estimation of Drotaverine Hydrochloride and Mefenamic Acid in combined dosage form.

Presented poster in GUJCOST sponsored 4th international Conference on "Theranostic Nanoparticles: A recent Breakthrough in Nanotechnology"at Shree Dhanvantary Pharmacy College, Kim (15th and 16th April 2016).

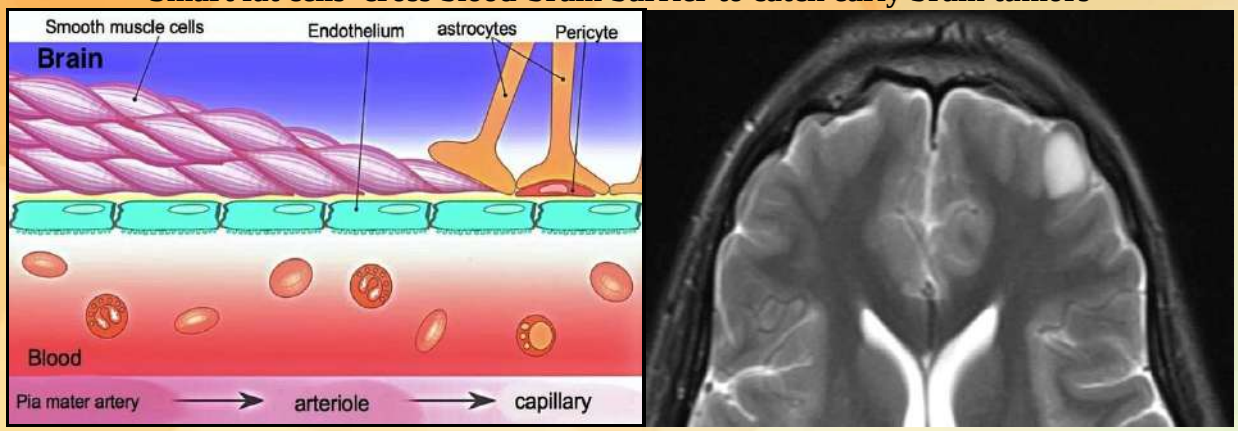
smart fat cells

"Smart fat cells" are able to cross the blood-brain barrier; something that regular Magnevist could not do unless the blood-brain barrier was damaged. This could be a better alternative to finding small tumors than another method being used: ultrasound. Ultrasound disrupts the blood-brain barrier which could allow other harmful things to pass into the brain. Scientists hope that these "smart fat cells" can also be used to deliver chemotherapy drugs along with the contrast chemicals so tumors can be found and destroyed all at once.

To find brain tumors, doctors inject people with a chemical that causes tumors to contrast, or "light up" on an MRI (magnetic resonance imaging). BUT, the chemical can only pass through the blood-brain barrier when the tumor has gotten big enough to damage the barrier. Patients with brain tumors can often survive the first brain tumor they get, but not the other, smaller tumors that reappear later, because the chemical used in MRI cannot detect them because they haven't damaged the blood-brain barrier yet. This is because the smaller secondary tumors are made up of cells that "survived" the first round of cancer treatment and spread to other parts of the brain. Scientists at Penn State University put the MRI contrast chemical Magnevist inside of liposomes (a tiny sac of fatty substances commonly used to deliver drugs to cells). The liposomes have proteins on them that attach to the cancer cells. They called these liposomes "smart fat cells". The scientists injected the liposomes into mice. They also injected the normal Magnevist contrast chemical into mice for comparison. They looked at the brains of the mice using MRI and looked at the images to see the difference between the brains of mice that had regular Magnevist injected in them and mice that had "smart fat cells" injected into them. Smart fat cells can help detect smaller, early-stage gliomas in mice before they become deadly. These tiny cells cross the blood-brain barrier, which protects the brain by blocking most molecules from entering it, and seek out the glioma tumor cells. Since these fat cells are also laded with a 'light up' agent, they show up on MRI scans, showing where the developing tumor is growing.An MRI contrast agent that can pass through the blood-brain barrier will allow doctors to detect deadly brain tumors called gliomas earlier. This ability opens the door to make this fatal cancer treatable. Gliomas are brain tumors that arise from glial cells, which help nerve cells to stay connected and send signals throughout the body. Cancerous gliomas are uniformly fatal, with a median survival rate of 14 months from the time of diagnosis. But a new nanotechnology approach developed by Xiaoli Liu and Madhan Kumar in the Department of Neurosurgery could transform gliomas from a death sentence into a treatable condition. Patients diagnosed with a malignant glioma can undergo surgery, chemotherapy and radiation to destroy the tumor, but the cancer will return. "Patients typically don't die from the tumor they initially presented with. Rather, they die from new tumors that come back in other parts of the brain," said James Connor, distinguished professor of neurosurgery. These new gliomas tend to grow quickly and are often resistant to treatment because they spring from cancer cells that survived the first therapeutic assault. Glioma patients have follow-up MRIs to detect new brain cancers but the tests do not catch the tumors early enough to save lives. That is because contrast agents used to outline gliomas on an MRI can only pass the protective blood-brain barrier once the tumors have grown large enough to cause damage to the barrier. Until then, the blood-brain barrier blocks 98 percent of small molecules and all large molecules from entering the brain. To overcome this deadly limitation, Penn State researchers created "smart fat cells" called liposomes that can pass the blood-brain barrier in mice, seek out tiny cancerous gliomas like heat-seeking missiles and light them up on an MRI. The liposomes are loaded with the most commonly used contrast agent, Magnevist. On their surface, the liposomes are studded with proteins that target receptors on glioma cells. The new contrast agent delivery system is more sensitive than traditional contrast-enhanced MRI, Connor said. The researchers found that the liposomes entered the brain in healthy mice with

uncompromised blood-brain barriers. Both techniques found large gliomas in mice with cancer, but only the liposome-encapsulated agent was able to detect smaller early-stage tumors.

Smart fat cells' cross blood-brain barrier to catch early brain tumors



It is not known exactly how the liposomes get past the intact blood-brain barrier, but they do it without causing damage. In the study, mice showed no harm from the treatment. This novel approach is an alternative to ultrasound, another promising method researchers are studying to get therapeutic agents into the brain. However, the ultrasound causes temporary disruption to the blood-brain barrier which allows not only the therapeutic agent to enter the brain, but also blood which could have medical implications. "Ultrasound, with all of its good qualities, is disruptive to the blood-brain barrier, whereas we can get an agent to cross it without causing disruption," Connor said. The researchers said that in the future, smart fat cells will deliver chemotherapeutic drugs, along with contrast agents, to brain tumor patients so that cancer cells can be detected and wiped out in one step. Scientists at Penn State University put the MRI contrast chemical Magnevist inside of liposomes (a tiny sac of fatty substances commonly used to deliver drugs to cells). The liposomes have proteins on them that attach to the cancer cells. They called these liposomes “smart fat cells”. The scientists injected the liposomes into mice. They also injected the normal Magnevist contrast chemical into mice for comparison. They looked at the brains of the mice using MRI and looked at the images to see the difference between the brains of mice that had regular Magnevist injected in them and mice that had “smart fat cells” injected into them. Scientists could see large tumors on the MRIs of both the mice injected with regular Magnevist and the mice injected with Magnevist-filled liposomes aka “smart fat cells”. Only the MRIs of mice injected with “smart fat cells” showed small tumors, though. No small tumors could be seen on the MRIs of mice injected with just Magnevist.

— **Article by Mrs.Kavita Sutariya (Asst. Professor)**

SMART PATCH FOR DIABETES AUTOMATICALLY LOWERS BLOOD SUGAR LEVELS

Scientists demostrated a new “smart cell patch” that quickly reduced and then maintained blood glucose at a stabilized level for more than 10 hours in diabetic mice . This patch is filled with natural beta cells that sense the body’s glucose signals and respond by secreting doses of insulin on demand to control blood glucose level, with no risk of inducing hypoglycemia. For decades, we have known that the transplantation of insulin producing cells to control the glucose level in the patients, yet only few of them have achieved normal blood glucose levels, as many of the transplantation were rejected and many of the medications used to suppress the immune system wind up interfering with the activity of beta cells and insulin. So, most recently attemption of an encapsulated beta cells into biocompatible polymeric cells that could be implanted in the body- the painless ‘smart insulin patch’. The patch requires no implantation because it’s applied to the

skin, and it's also outside the immune system. This study provides a potential solution for the tough problem of rejection,which has long plagued studies on pancreatic cell transplants for diabetes. The 'smart cell patch' which is no bigger than a postage stamp,is covered on one side with an array of 400 microneedles- each only 800µm in length. The microneedles are composed of hyaluronic acid and packed with thousands of pancreatic beta cells and glucose amplifiers. When the patch is applied, the microneedles poke through the skin into capillaries and blood vessels, forming a connection between internal environment and the external cells of patch. During hyperglycemia, the glucose,signal amplifiers,which are made of hypoxia,sensitive materials,respond to the rapid glucose oxidation by quickly releasing encapsulated enzymes. These enzymes diffuse into the external positioned beta cell capsule,which acclerates their secretion of insulin into the capillaries and vessels. In experiments in a mouse model of diabetes,the scientists showed that patch quickly lowered blood glucose in the mice to normal levels. Next, the researchers sought to verify that the patc could regulate blood glucose without lowering it too much,so they administered a second patch to the mice at 6 hours after the first one, as repeated administration did not result in excess doses of insulin, and thus did not risk hypoglycemia. Instead, the second patch extended the life of the treatment to 20 hours. These results provide a proof of principle for an alternative approach that could be safer and less cumbersome than current insulin treatments.

— **QADRI MISBAH SYED NIZAMUDDIN**
(6th Semester B.pharm)

Stem Cell Therapy: A Comprehensive Review

Stem cells are master cells. It is a raw material from which all of the body's mature, differentiated cells are made. It gives rise to brain cells, nerve cells, heart cells, pancreatic cells etc. This are undifferentiated cells can differentiate to yield major specialized cell types or organs. It has cell renewal property which may be useful to maintain and repair the tissue. Thus they have potential to replace cell tissue damage by severe illness.

Hemotopoietic stem cell transplantation (HSCT)
Stem cells that give rise to the lymphocytes and other cells of the immune system, also make blood, are called hematopoietic stem cells. HSC's are characterized by the presence of CD 34 antigen.The process of taking stem cells from one person and putting them into another is called HSCT.To treat cancer patients with conditions such as leukemia and lymphoma, sickle cell anaemia.In restoring the haematopoietic system

Stem cells in treating baldness:
As hair follicles contain stem cells- dermal papilla**.**Take stem cells from existing hair follicles**.**Multiply them in culture**.**Implant the new follicles into the scalp.

Diabetes: In diabetes, there is loss of insulin-producing beta cells of the pancreas. Human embryonic stem cells may be grown in cell cultures and stimulated to form insulin- producing cells, that can be transplated into the patient. Pancreas is digested with collagenase that frees islets from the surrounding cells.Centrifugation of isolates containing mainly alpha and beta cells.Then purified islets beta cells.And transplanted through a catheter into the live where they become permanantly established.

— Zeba Shaikh
(6th Semester B.pharm)

HOBBY CORNER

"Proud of You"

Tears came in her eyes. Mini got shocked by seeing her scorecard this morning as it was hard to digest the fact. She felt like the time has stopped. She lost two Subjects in std. 10. Letting her tears fall down, she now covered up with nervousness and fear. For the first time in life she didn't want to go home. Her brother stood first in school in std.12, which made her even more loose. She was scolding herself for the results. She started imagining pappa's response.

"Pa", probably the word she loved the most. He always loved her a lot, put confidence in her and ever proved the best father and what about her? She made him down today. Her tears again started shading her result card.

Every year pa takes them to ice-cream parlour. She thought for those wonderful moments and smile came on her face but quickly vanished. Now it was a time to go home. She and her brother reach home. As expected pa came early from office. Taking his son's hand, he praised him, hug him and felt proud which could be seen from his face. Now it was mini's turn. She thought for a moment that what if the grade card would disappear? Or some numerical magic happen to it. She closed her eyes and did not want to open ever. Pa called her and to her surprise he smiled with tears in his eyes. Kissing her forehead he said " **I am proud of you dear**". The words still were echoing in her ears. Mini astonishingly looked at him and become curious to know what have happened? Why pa responded unusually? Did the magic really happen with the score card? Finally she courageously asked, why pa? Please carefully see my result.

Pa replied, "Yes" I know you got failed to clear two subjects. Now it was a time for mini to get surprised. Pa continued, "Dear" two days back 'shanti' our maid, came to thank me. You know for what? She told that you shared your Tiffin with her daughter working in a nearby book store as shanti was hospitalized for a week. Yesterday Rima's mother came home saying you paid her examination fees from your pocket money and that is why she could appear in an exam. Today morning your mother told that you kept water pots in our windows and balcony for birds.

"Dear daughter", he said." I am so happy for your deeds and now me and your mother don't want you to become a topper or score highest in the class. We will be happy if you study well but we will feel happiest ever if you continue "being human" and of course, "we are proud of you". "I am sure you and your brother this time will give us an ice cream party from your pocket money". All laughed, this time with tears of happiness in mini's eyes.

– **Story by Dr. Bhumika Desai. (Asst. Professor)**

Painting by Archi Patel. 2nd Semester B.pharm

DEDICATION TO SENIORS

The words I would like to dedicate to our seniors on there farewell.. ‘’as we all are honoured and humbled to have an opportunity to bid a farewell to our seniors. On behalf of all of us i would like to congratulate each and everyone of you on the great success at this university.’’

‘’ I remember thinking that for you all its not the goodbye that hurts but the flashback that follows”. I still remember the first meeting with our seniors and telling the truth that they had really put a great efforts in boosting our confidence level and diminishing the communication gap among us. Although we may be separated by time and distance in the interim, nothing will diminish the important role that you all have. So i would like to say that

Sing us no song, tell us no tales,
Cry us no tears, but remember us kindly.

“The only thing that make leaving college bearable is the hope against hope that you all are taking the best part of your life with you”.

Now, FAREWELL it is...
A friend and more, you have been so good, All time happy or sad, with us you stood!
The care that you all showered, the time that you all rendered!
Never felt so safe, we had it all figured!
You all would stay, you all would be here,
least I ever thought, this time will be so near!
Getting far or beyond, just tears with no sound,
had you ever known? you will be so important on this ground.
Thanks. to all the time for it, Gave us such a wonderful friends, not words can describe to, what extend you let us depend.
All the happiness be yours, let all the success come your way,
remember us in your needs , we’ll be just a call away.
DONT CRY BECAUSE IT OVER, SMILE BECAUSE IT HAPPENED..

– Qadri Misbah Syednizamuddin
– (6th Semester B.pharm)

Glass Painting by Namrata Thakor, 2nd Semester B.pharm

Glass Painting by Krishna Rangrej, 2nd Semester B.pharm

Money Cover with Quilling design by Riddhi Shah, 2nd Semester B.pharm

POEMs

POEMs

LIVING BEYOND LIVING

Day comes day goes
turning some parts of us
into shadows;

coal when burnt
turns ash;
days when spent
also crash;

age is a junkyard
a million dreams realized
and dumped aside;

God is God
because he is still a mystery;
Otherwise, he would just be
a forgotten chapter
in a school syllabus;

past and present
do not matter;
no one wants the present
to extend beyond a tiny moment;

the sky and the earth
represent the future;
the unlimited, the unknown,
the mysterious spreading around;

from where, we are
to pick our destiny and carve out
features which belong to us.

– Patil Vishal
(Lecturer)

POEM OF PHARMACIST

P eople in pain can be cross as a rule
H owever, the pharmacist helps them keep their cool
A lways your friend, he often gives free advice
R emember his service when you consider the price
M any years he has trained before he could start
A nd more importanatly, he's got a great big heart
C ertainly his is the most trusted profession
I t's your health that is his obsession
S o the next time you see him, give him a smile
T reat him nicely, you'll get it back by a mile
S urely, he'll keep you healthy, at least for a while!

– Poem by Arti B. Patel.
(Asst.Professor)

TRY AGAIN

HAVE YOU TRIED ONCE MORE AND FAILED?
TRY AGAIN……..
HAS DESPAIR YOU HEART ASSAILED?
TRY AGAIN…….
DON'T GIVE UP, HAVE COURAGE STILL
HOW WILL YOU CONQUER, SAY "I WILL"
YOU MAY GET YOUR HOPES FULFIL,
TRY AGAIN……..
BE PERSISTANT, DO NOT QUIT
TRY AGAIN……..
SPEEDY HOW TO WIN SUCCESS,
DON'T LEAVE ANYTHING TO CHANCE,
WINNING WILL MEANS HAPPINESS…….
TRY AGAIN……..
STICK TO WHAT YOU HAVE BEGUN…….
TRY AGAIN……..
DON'T LEAVE ANYTHING HALF DONE……..
TRY AGAIN……..
LOOK ON FAILURE AS A TEST
NEVER STOP AND TAKE A RISK
TILL YOU KNOW YOU'VE DONE YOUR BEST……

– Poem by Jha Shivam
4th semester B.Pharm.

EXTRA-CURRICULAR ACTIVITIES

SPORTS WEEK CELEBRATION

Box Cricket on 15th Feb, 2016

Kho-Kho on 16th Feb, 2016

Bedminton on 17th Feb, 2016

Cricket on 17th & 18th Feb, 2016

Kabaddi and Volleyball on 19th Feb, 2016

Review Article

Thiazolidinediones against Diabetes and Cancer

Dr. Mahesh G. Saralai, Ms. Shivali B. Desai*

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Abstract

Insulin resistance both precedes and predicts type 2 diabetes mellitus. The insulin sensitizing thiazolidinediones, which are selective ligands of the nuclear transcription factor peroxisome-proliferator-activated receptor γ (PPARγ), are the first drugs to address the basic problem of insulin resistance in patients with type 2 diabetes. Epidemiological studies clearly indicate that the risk of several types of cancer (including pancreas, liver, breast, colorectal, urinary tract, and female reproductive organs) is increased in diabetic patients. Mortality is also moderately increased. Hyperinsulinemia most likely favors cancer in diabetic patients as insulin is a growth factor with pre-eminent metabolic but also mitogenic effects, and its action in malignant cells is favored by mechanisms acting at both the receptor and post-receptor level. While anti-diabetic drugs have a minor influence on cancer risk (except perhaps the biguanide metformin that apparently reduces the risk), drugs used to treat cancer may either cause diabetes or worsen a pre-existing diabetes. In addition to the well-known diabetogenic effect of glucocorticoids and anti-androgens, an increasing number of targeted anti-cancer molecules may interfere with glucose metabolism acting at different levels on the signaling substrates shared by IGF-I and insulin receptors. In addition to their known insulin sensitization action, thiazolidinediones have been shown to suppress tumor development in several *in vitro* and *in vivo* models. Among the proposed mechanisms for the anti-tumor effects of TZDs, apoptosis induction, cell cycle arrest, and differentiation have been extensively reported. Interestingly, some of the observed anti-tumor effects are independent of PPAR-γ activation.

Keywords: Thiazolidinediones, Diabetes, Cancer, Apoptosis, PPAR- γ

INTRODUCTION

Thiazolidinediones (TZDs) are a class of antidiabetic drugs which include pioglitazone, rosiglitazone, ciglitazone and troglitazone, although troglitazone was removed from the market in 2000 because of hepatoxicity. TZDs bind with high affinity to the PPAR-gamma (PPAR-γ) subtype of peroxisome-proliferator activated receptors (PPARs). PPARs are members of the steroid receptor superfamily of ligand-activated transcription factors. Upon activation, either by synthetic ligands such as TZDs, or endogenous ligands such as natural lipophilic ligands (e.g. fatty acids), PPAR-γ forms a heterodimer with the retinoid X receptor (RXR) and binds to PPAR response elements (PPRE) that regulate the transcription of select target genes. The complexity of PPAR-γ - regulated gene expression is enhanced by various co-activators and co-repressors that are recruited to the transcriptional complex by the activated PPAR-γ heterodimer.[1] Ligands differ in their ability to inter-act with coactivators, which explains the various biologic responses observed. A second mechanism, transrepression, may explain the antiinflammatory actions of PPARs. It involves interfering with other transcription-factor pathways in a DNA-independent way.[2] second mechanism, transrepression, may explain the antiinflammatory actions of PPARs. It involves interfering with other transcription-factor pathways in a DNA-independent way.[3] Two PPAR-γ isoforms exist that are derived from the alternate promoters, PPAR-γ1 and PPAR- γ2. The PPAR-γ2 isoform is 30 amino acids longer than PPAR-γ1 and is less abundant.

Two PPAR-γ isoforms exist that are derived from the alternate promoters, PPAR-γ1 and PPAR- γ2. PPAR-γ2 is predominantly expressed in adipose tissue where it exerts pleiotropic effects on metabolism, insulin sensitization, and inflammation. PPAR-γ2 is also expressed in vascular endothelium, suggesting a role for this protein in vascular biology as well as in alveolar macrophages[5,6]. In contrast, PPAR-γ1 is expressed in a broad variety of tissues including large intestine, kidney, liver, skin and brain. PPAR-γ has been detected in cancer cells.[7] Several reports have demonstrated that PPAR-γ activation has anti-cancer properties. For example, TZDs suppress tumor development in several animal models, and PPAR-γ activation arrests malignant cell growth.[8]In addition, treatment of cancer cells with PPAR-γ-activating TZDs induces cell differentiation and apoptosis [9].

THE SUPERFAMILY OF PEROXISOME-PROLIFERATOR–ACTIVATED RECEPTORS

The peroxisome-proliferator–activated receptors (PPARs) are a subfamily of the 48-member nuclear-receptor superfamily and regulate gene expression in response to ligand binding. Various fatty acids serve as endogenous ligands for PPARs, whereas some members of the superfamily (farnesoid X receptors) bind bile acids and others (liver X receptors) bind oxysterols. Three PPARs, designated PPARα, PPARδ (also known as PPARβ and PPARγ, have been identified to date.

After ligand binding, PPARs undergo specific conformational changes that allow for the recruitment of one coactivator protein or more.[8] Ligands differ in their ability to interact with coactivators, which explains the various biologic responses observed. PPARs regulate gene transcription by two mechanisms (Fig. 1). Transactivation is DNAdependent and involves binding to PPAR response elements of target genes and heterodimerization with the retinoid X receptor.[8] A second mechanism, transrepression, may explain the antiinflammatory actions of PPARs. It involves interfering with other transcription-factor pathways in a DNA-independent way.

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PPAR*a* is expressed predominantly in the liver, heart, and muscle, as well as in the vascular wall. Fibrates such as fenofibrate, bezafibrate, ciprofibrate, and gemfibrozil act as full or partial PPAR*a* agonists. In general, PPAR*a* activation enhances free fatty acid oxidation, controls expression of multiple genes regulating lipoprotein concentra-tions, and has anti-inflammatory effects (Fig.2). PPAR*a* agonists prevent or retard atherosclerosis in mice and humans.[12-14]

PPAR*δ* is expressed in many tissues, with the highest expression in the skin, brain, and adipose tissue. In mice in which PPAR*d* is ablated (PPAR*δ* null mice),[15] these tissues display alterations such as delayed wound closure and diminished myelination.

PPAR*g* is expressed most abundantly in adipose tissue but is also found in pancreatic beta cells, vas-cular endothelium, and macrophages.[8,16] Its ex-pression is low in tissues that express predominant-ly PPAR*a*, such as the liver, the heart, and skeletal muscle. The discovery of PPAR*g* as the target for thiazolidinediones was followed by large-scale clin-ical trials of several agents.[17-27] In January 1997, the first thiazolidinedione, troglitazone, was approved as a glucose-lowering therapy for patients in the United States with type 2 diabetes. Troglitazone was subsequently withdrawn from the market, in March 2000, because of hepatotoxicity. The two currently available PPAR*g* agonists, rosiglitazone and piogli-tazone, were approved in the United States in 1999.

MECHANISM OF ACTION OF THIAZOLIDINEDIONES[28]

Insulin sensitivity and secretion

Thiazolidinediones consistently lower fasting and postprandial glucose concentrations as well as free fatty acid concentrations in clinical studies. In-sulin concentrations also decrease in most stud-ies. Such changes indicate that thiazolidinedi-ones act as insulin sensitizers, which has been confirmed by direct measurements in in vivo studies in humans. For example, treatment of nondiabetic subjects or those with type 2 diabetes for three to six months with troglitazone, rosiglitazone, or pioglit-azone increases insulin-stimulated glucose uptake in peripheral tissues. In similar studies, thiazolidinediones increase hepatic insulin sensi-tivity (the ability of insulin to suppress endogenous glucose production) and insulin sensitivity in adi-pose tissue (measured from the ability of insulin to suppress free fatty acid concentrations). In addi-tion, insulin secretory responses, even after adjust-ment for an improvement in insulin sensitivity, have increased in subjects with impaired glucose toler-ance and type 2 diabetes. Somewhat paradox-ically, these improvements are generally accom-panied by weight gain and an increase in the subcutaneous adipose-tissue mass.

Enhancement of insulin sensitivity

PPAR*g* is essential for normal adipocyte differenti-ation and proliferation as well as fatty acid uptake and storage. Thiazolidinediones increase the num-ber of small adipocytes and the subcutaneous ad-ipose-tissue mass in studies in animal mod-els.[11] These observations, plus the high level of PPAR*g* expression in adipose tissue, have led to the hypothesis that thiazolidinediones exert their insulin-sensitizing actions either directly (the “fat-ty

acid steal" hypothesis) or indirectly, by means of altered adipokine release, modulating insulin sensitivity outside adipose tissue. According to the "fat-ty acid steal" hypothesis, thiazolidinediones pro-mote fatty acid uptake and storage in adipose tissue. In this way, they increase adipose-tissue mass and spare other insulin-sensitive tissues such as skeletal muscle and the liver, and possibly pancreatic beta cells, from the harmful metabolic effects of high concentrations of free fatty acids. Thiazolidinedi-ones thus keep fat where it belongs.

In a manner consistent with that hypothesis, thiazolidinediones lower circulating free fatty acid concentrations and triglyceride content in the liver, but not in skeletal muscle, in patients with type 2 diabetes and lipodystrophy. Metformin increases insulin sensitivity in the liver without changing its fat content in patients with type 2 dia-betes, and thiazolidinediones can lower fasting in-sulin concentrations without increasing subcuta-neous fat mass in patients with lipodystrophy.

In mice, targeted deletion of PPAR*g* in adipose tissue does not induce insulin resistance in mus-cle, whereas muscle-specific PPAR*g* deletion does cause such resistance. Insulin resistance in mus-cle is unresponsive to thiazolidinediones, implying that these agents sensitize by directly stimulating muscle PPAR*g* receptors. Hepatic insulin resis-tance in mice lacking PPAR*g* in adipose tissue can be reversed with thiazolidinediones.

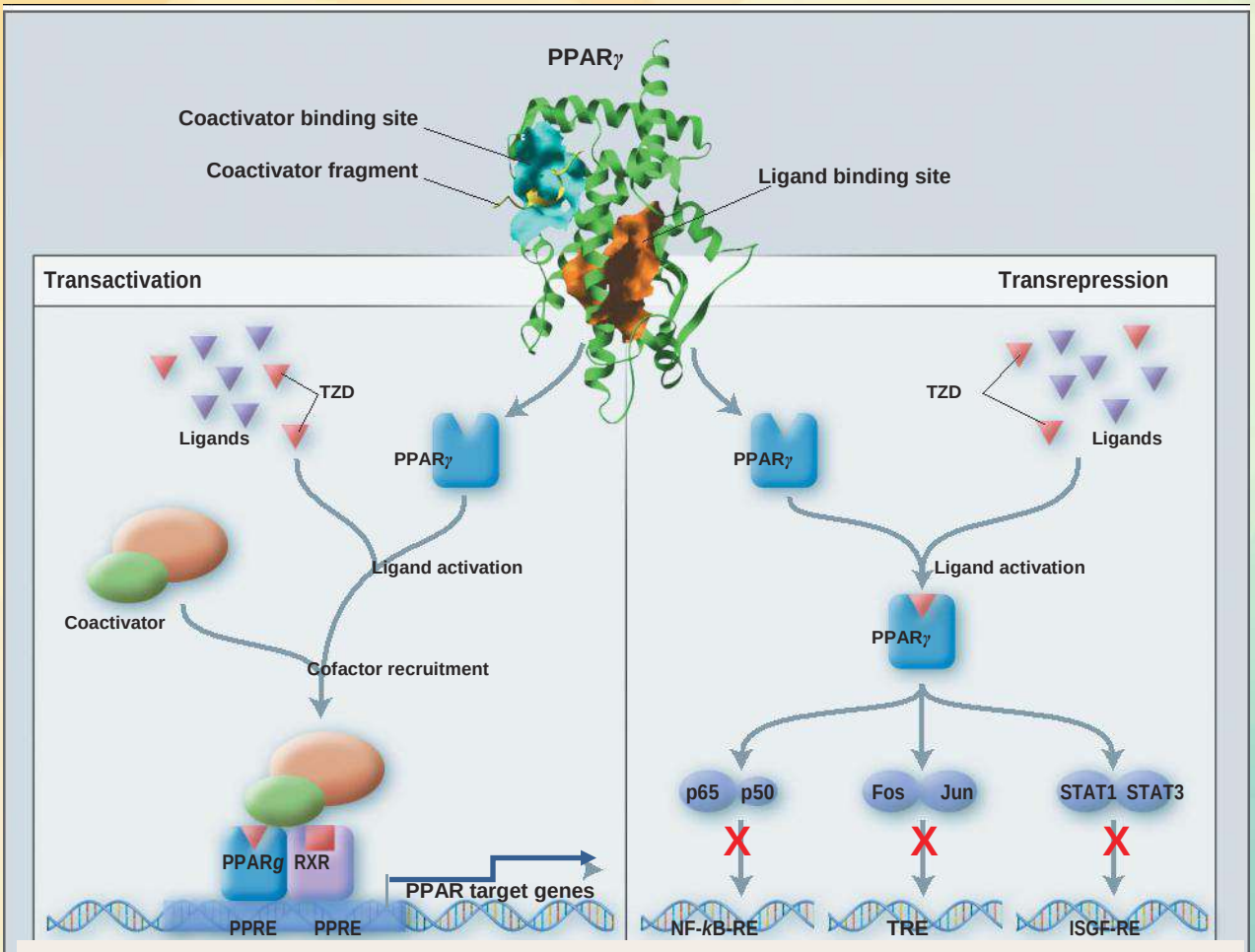

Figure 1. Molecular Mechanisms of Biologic Responses of Thiazolidinediones.
Peroxisome-proliferator–activated receptor *g* (PPAR*g*) is a transcription factor activated by thiazolidinediones (TZDs). In transactivation, which is DNA-dependent, PPAR*g* forms a heterodimer with the retinoid X receptor (RXR) and recognizes specific DNA response elements called PPAR response elements (PPRE) in the promoter region of target genes. This results ultimately in transcription of PPAR*g* target genes. After ligand binding, PPARs undergo conformational changes, which lead to recruitment of cofactor proteins and coactivators. The coactivators interact with nuclear receptors in a ligand-dependent way and influence the set of genes transcribed. In transrepression, PPARs can re-press gene transcription by negatively interfering with other signal-transduction pathways, such as the nuclear factor-*k*B (NF-*k*B) signaling pathway, in a DNA-binding–independent manner. STAT denotes signal transducers and activators of transcription, ISGF-RE interferon-stim-ulated gene factor responsive element, and TRE TPA responsive element, where TPA is a phorbol ester.

These data suggest that the insulin-sensitizing effects of thiazolidinediones in the liver and muscle of mice are not mediated by PPAR*g* receptors in adipose tissue in cases in which adipose tissue is unable to respond to these agents normally. However, the lipoatrophy that accompanies tissue-specific PPAR*g* deletion may make the action of PPAR*g* agonists abnormally dependent on PPAR*g* expression in other tissues. For example, rosiglitazone is able to reverse hyper-triglyceridemia, hyperglycemia, and hyperinsulin-emia in normal mice, whereas the drug is ineffective in lipoatrophic mice. Taken together, data from knockout-mouse models support the idea that adi-pose tissue is the most important site for thiazo-lidinedione action if there are normal amounts of adipose tissue.

Indirect effects in adipose tissue

Although thiazolidinediones may enhance insulin sensitivity by keeping fat where it belongs, indirect effects may also be involved. Gene-expression pro-filing studies using oligonucleotide microarrays in differentiated 3T3-L1 adipocytes have indicated that rosiglitazone and pioglitazone each regulate the ex-pression of more than 100 genes and that these genes are not identical, although they cluster togeth-er.[10] A small fraction of the established PPAR*g* tar-get genes that also seem to be regulated in human adipose tissue in vitro are shown in Figure 2. Various adipokines, such as adiponectin, tumor necrosis factor *a*, resistin, and 11*b*-hydroxyster-oid dehydrogenase 1, the enzyme that produces cor-tisol locally in adipose tissue,[11] are among the genes that are regulated by PPAR*g* agonists in ro-dents. Of these, adiponectin increases insulin sen-sitivity, and tumor necrosis factor *a*, resistin, and 11*b*-hydroxysteroid dehydrogenase 1 induce in-sulin resistance in rodents.

Adiponectin, an adipocytokine produced exclu sively by adipose tissue, has both insulin-sensitizing and antiatherogenic properties in mice. PPAR*g* agonists increase adiponectin expression in vitro in adipose tissue. Adiponectin levels are low in pa-tients with obesity and type 2 diabetes, as well as in patients with lipodystrophy. In vivo treat-ment with thiazolidinediones markedly increases circulating concentrations of adi-ponectin, the most abundantly expressed gene transcript in human adipose tissue. It is unclear whether adiponectin increases hepatic insulin sensitivity in humans as it does in mice, although plas-ma adiponectin concentrations correlate with liver fat content both before and after thiazolidinedione treatment in patients with type 2 diabetes.

In the liver and in adipose tissue, 11*b*-hydroxy-steroid dehydrogenase 1 catalyzes the interconver-sion of cortisone to cortisol. A full-blown meta-bolic syndrome characterized by obesity and the accumulation of visceral fat, as well as increased concentrations of cortisol in the portal vein but not of systemic cortisol, develops in mice that overex-press 11*b*-hydroxysteroid dehydrogenase 1 in adi-pose tissue. Thiazolidinediones down-regulate 11*b*-hydroxysteroid dehydrogenase 1 expression in adipose tissue and might thereby alleviate features of the metabolic syndrome. However, no data on the effects of thiazolidinediones on 11*b*-hydroxy-steroid dehydrogenase 1 activity or expression in humans are available.

The many effects of thiazolidinediones in vari-ous tissues make it impossible to define the exact mechanisms underlying their insulin-sensitizing effects in vivo in humans. Data suggest that multi-ple mechanisms are probably involved (Fig. 3). One mechanism includes stimulation of free fatty acid storage in adipose tissue, sparing other tissues such as the liver, skeletal muscle, and possibly beta cells from lipotoxicity. These drugs may also have indirect insulin-sensitizing effects, especially in the liver by means of the secretion of adiponectin from adipose tissue.

CLINICAL EFFICACY OF THIAZOLIDINEDIONES IN HUMANS[28]

Effects in patients with type 2 diabetes

Rosiglitazone and pioglitazone are currently approved in most countries for the treatment of hyperglycemia in patients with type 2 diabetes, either as monotherapy or in combination with sulfonyl-ureas or metformin. In the United States, both drugs have also been approved for use in combi-nation with insulin, provided certain precautions are followed.

Hypoglycemic effects

Placebo-controlled studies suggest that both pio-glitazone and rosiglitazone are moderately effective in achieving glycemic control (Table 1). At maximal doses, these two drugs seem to decrease glycosy-lated hemoglobin values on average by 1 to 1.5 per-cent. Thus, in a typical patient with type 2 diabetes, one may expect glycosylated hemoglobin to de-crease from a value of 8.5 percent to a value of 7 per-cent (normal range, 4 to 6 percent). Pioglitazone and rosiglitazone decrease glycosylated hemoglo-bin values more than the weakest hypoglycemic drugs(e.g., nateglinide and *a*-glucosidase inhibi-tors) but slightly less than full doses of glimepiride (4 to 6 mg), glyburide (glibenclamide, 10 to 15 mg), or metformin (2 to 2.5

g). Whether thiazoli-dinediones are used as monotherapy or are added to existing therapies does not seem to affect their hypoglycemic efficacy. No data are available on pa-tient characteristics that can predict a good treat-ment response, and no data are available to support long-term maintenance of glycemic control with rosiglitazone or pioglitazone as compared with oth-er existing therapies. Ongoing studies may be use-ful, such as the A Diabetes Outcome Progression Trial (ADOPT), which involves patients with type 2 diabetes who have not previously received treat-ment and who have been randomly assigned to re-ceive rosiglitazone, glyburide, or metformin monotherapy.

Effects on lipids

There are no head-to-head double-blind studies comparing the effects of pioglitazone and rosiglit-azone on serum lipids and lipoproteins. However, low-density lipoprotein (LDL) cholesterol levels have consistently remained unchanged when monother-apy with pioglitazone or combination therapy with pioglitazone and sulfonylurea, metformin, or insu-lin has been used. In contrast, increases in LDL cho-lesterol levels, ranging from 8 to 16 percent, have been noted in studies of rosiglitazone (Fig. 4). High-density lipoprotein (HDL) cholesterol levels have increased by approximately 10 percent with both drugs.

The effects of thiazolidinediones on triglycerides have been somewhat more variable. Decreases in triglyceride levels have been observed more often with pioglitazone than with rosiglitazone

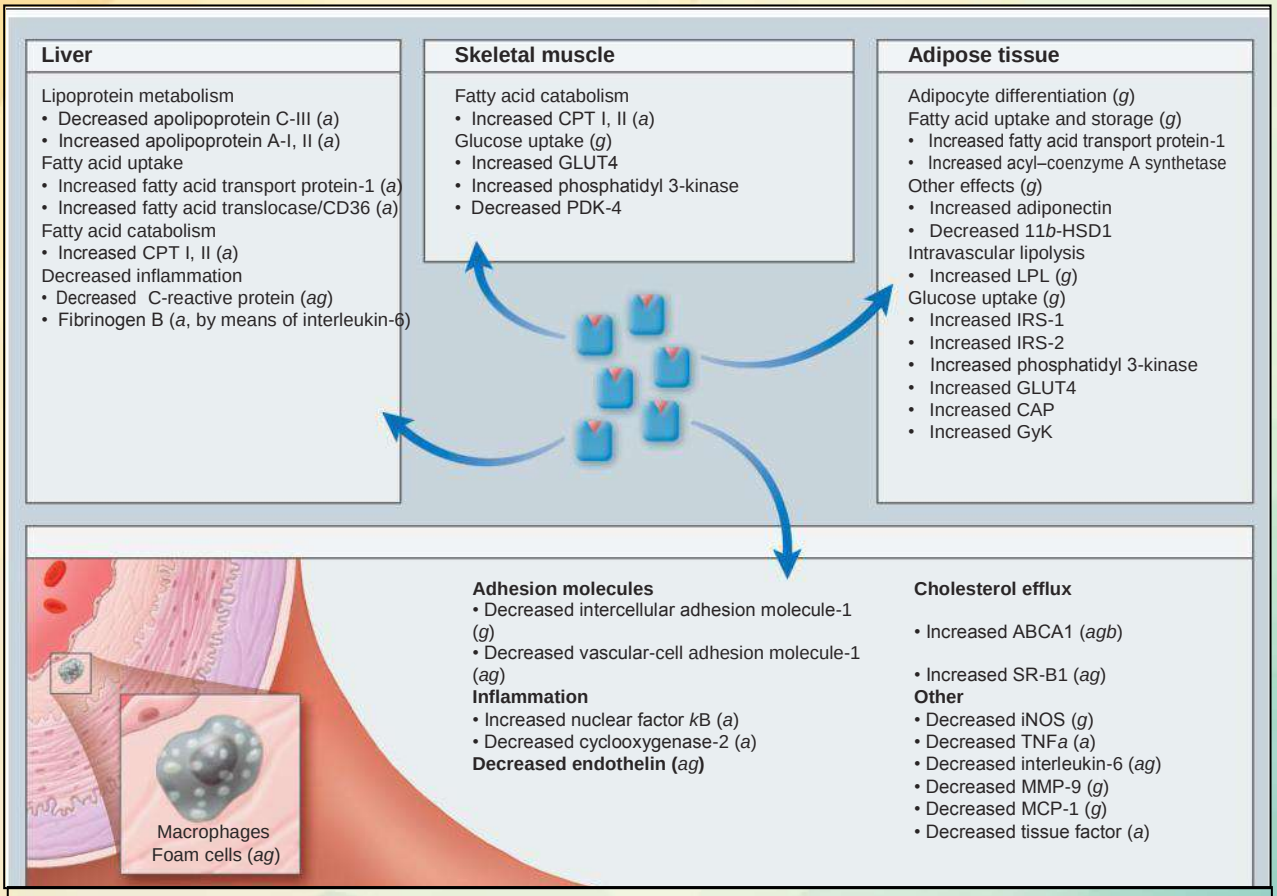

Figure 2. Molecular Targets of PPAR*g* and PPAR*a* Action.

PPAR*a* is expressed mainly in the liver, in skeletal muscle, in the heart (not shown), and in the endothelial cells and smooth-muscle cells of the vascular wall. It regulates genes that influence lipoprotein metabolism and fatty acid uptake and oxidation as well as production of inflam-matory markers. PPAR*g* is expressed mainly in adipose tissue, where it regulates genes involved in adipocyte differentiation, fatty acid uptake and storage, and glucose uptake. It also stimulates intravascular lipolysis. CPT denotes carnitine palmitoyl transferase, *a* regulation of the gene by PPAR*a* agonists, *g* regulation of the gene by PPAR*g* agonists, *b* regulation of the gene by PPAR*b* (PPAR*d*) agonists, GLUT4 insulin-sensitive glucose transporter, PDK-4 pyruvate dehydrogenase kinase 4, HSD1 hydroxysteroid dehydrogenase type 1, LPL lipoprotein lipase, IRS insulin-receptor substrate, CAP Cbl–associated protein, GyK glycerol kinase, ABCA1 ATP-binding cassette A1, SR scavenger receptor, iNOS in-ducible nitric oxide synthase, TNF-*a* tumor necrosis factor *a*, MMP-9 matrix metalloproteinase 9, MCP-1 monocyte chemoattractant protein 1, and TZD thiazolidinedione.

The only direct comparison of rosiglitazone and pioglitazone in an open-label trial, in 127 patients previously treated with troglitazone, supports the idea that the two agents have similar effects on glycemia and body weight. The same study showed that pioglitazone is more effective than rosiglita-zone in regard to LDL cholesterol and serum triglyceride levels. The difference between the effects of the drugs on lipids cannot be attributed to differ-ences in their effects on serum free fatty acid con-centrations, which decreased by similar amounts, approximately 20 to 30 percent. Pioglitazone seems to act like a partial PPAR*a* agonist in vitro, whereas rosiglitazone seems to be a pure PPAR*g* agonist.

Data on mechanisms underlying the effects of the thiazolidinediones on lipids in humans are vir-tually nonexistent. For example, there are no data to characterize the effects of thiazolidinediones on the production and removal of lipoprotein particles containing apolipoprotein A-I or apolipopro-tein B. The cause of the increase in HDL and LDL cholesterol levels during rosiglitazone treatment is therefore unknown. The effects of rosiglitazone or pioglitzone on the size of LDL particles have not been studied in a double-blind, placebo-controlled trial. Rat and mouse models are not ideal for the study of human lipoprotein metabolism, because impaired clearance is the principal defect responsi-ble for hypertriglyceridemia in these models, rather than overproduction of very-low-density lipopro-teins, which is the case in humans.

DIABETES AND CANCER[29]

In diabetic patients, cancer may be favored by: i) general mechanisms that promote cancer initiation or progression in any organ because they are due to alterations (i.e. hyperglycemia or hyperinsulinemia or drugs) that affect all tissues; and ii) site-specific mechanisms affecting cancerogenesis of a particular organ.

Type-1 and Type-2 Diabetes and Cancer Risk

DM is a group of metabolic disorders characterized by hyperglycemia. The two most frequent subtypes of DM differ in both metabolic and hormonal charac-teristics: in type 1 diabetic patients (5–10% of all diabetics), hyperglycemia is associated with an absolute deficiency of endogenous insulin secretion and the absolute requirement for exogenous insulin administration.

In type 2 diabetes, hyperglycemia and hyperinsuli-nemia coexist for a long time because of insulin resistance in peripheral tissues. Only when b-cell function fails completely will the patient require insulin treatment because of endogenous insulin deficiency.

In spite of these considerable pathogenetic and clinical differences, many studies on the association between diabetes and cancer were carried out without an appropriate distinction between the two forms of diabetes.

For obvious epidemiological reasons, most studies on the association between cancer and diabetes have been carried out in patients with type 2

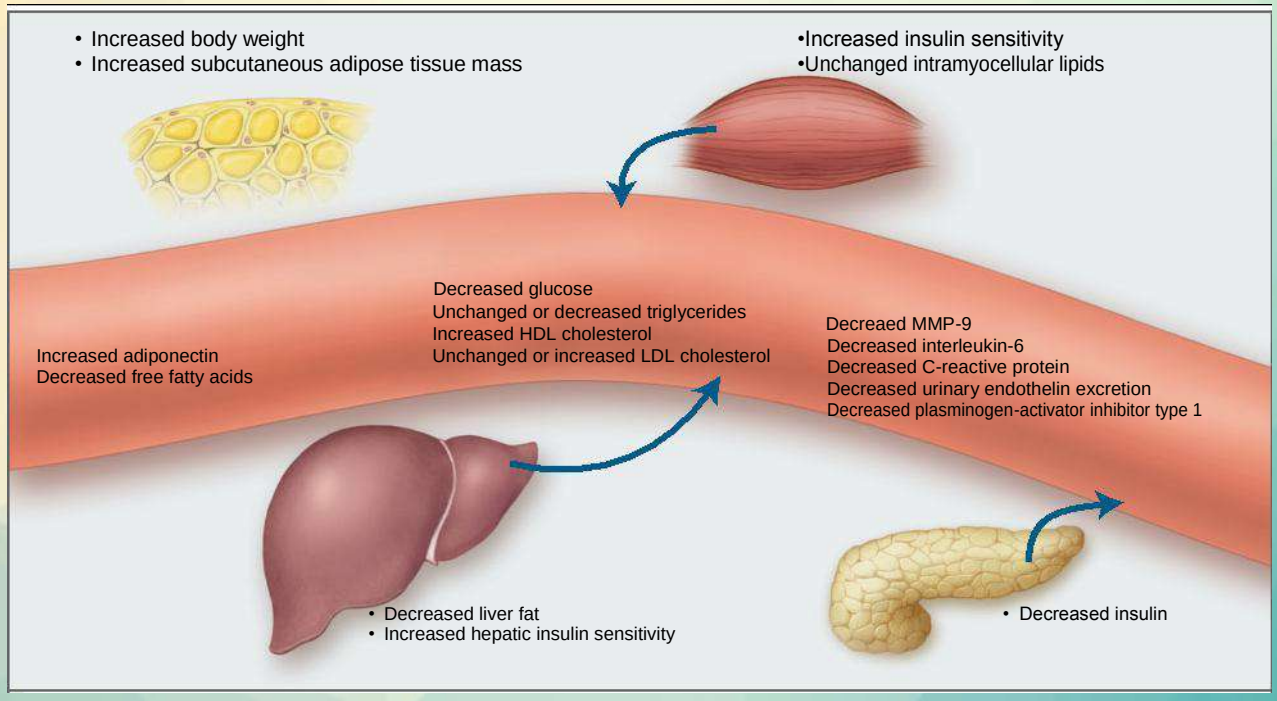

Figure 3. Mechanism of Action of Thiazolidinediones in Vivo in Humans.

diabetes (90% of all diabetic patients). As these patients, unlike those with type 1 diabetes, have endogenous hyper-insulinemia and insulin resistance, it is questionable whether these data can be automatically extended to type1 diabetic patients.

This concern is particularly relevant for the older reports in which diabetes assessment was based on self-reported hyperglycemia, with no criteria aimed at distinguishing type 1 from type 2 diabetes. Although more recent studies have been based on medical records, the distinction between type 1 and type 2 diabetes was mostly based on surrogate indicators of diabetes type, like young patient age or insulin treatment (assumed as type 1) versus insulin-independent diabetes (assumed as type 2). This distinction does not take into account many specific conditions, including type 2 diabetic patients that are treated with insulin because oral hypoglycemic agents (OHA) are no longer effective (secondary failure to OHA), type 1 diabetes of the adult (w5% of adult subjects previously classified as type 2 diabetes), and other less frequent conditions.

Because of the 10:1 ratio between type 2 and type 1 diabetes, and considering that cancer is mainly a disease of the older population (where type 1 diabetes is less frequent), it is reasonable to assume that the large majority of tumors observed in diabetic patients occurred in type 2 diabetics.

Thus, if cancer association with type 1 diabetes has specific characteristics, these have likely been obscured by the large majority of cancers diagnosed in type 2 diabetic patients.

In conclusion, the large majority of the epidemio-logical data on cancer incidence and mortality has been obtained in type 2 diabetic patients. Because of the different biology between the two subtypes of diabetes, these findings cannot be acritically extended to type 1 diabetic subjects.

The role of hyperinsulinemia in favoring cancer incidence and progression in diabetic patients

A role for insulin in promoting cancer growth was first recognized by studies in experimental animals. Rats and mice made diabetic with streptozotocin or alloxan (therefore hyperglycemic and insulin deficient) developed less aggressive tumors as they display a longer latency period for cancer development, lower number of tumors, slower cancer progression, and smaller final tumor volume with respect to control animals. Insulin treatment reversed these effects. These results are in concert with the well-known mitogenic effect of insulin that has been extensively documented both in vitro and in vivo.

Most type 1 and type 2 diabetic patients are exposed for decades to increased insulin concentrations, although the physiologic and therapeutic conditions are very different in each individual with diabetes.

Type 1 diabetic patients have an absolute require-ment for exogenous insulin because of autoimmune destruction of their pancreatic b-cells, which are therefore unable to produce endogenous insulin. In these patients, insulin administration cannot mimic the physiologic insulin secretion, not only in terms of temporal pattern and hormone serum levels but also in terms of compartment distribution. Indeed, pancreas-secreted insulin is first

Table 1: Meta-analyses on the relative risk (RR) of cancer in different organs of diabetic patients

Cancer	Case Study	RR (95% CI)	
Liver (El-Serag et al. 2006)	13 case–control studies	2.50	(1.8–3.5)
	7 cohort studies	2.51	(1.9–3.2)
Pancreas (Huxley et al. 2005)	17 case–control studies	1.94	(1.53–2.46)
	19 cohort studies	1.73	(1.59–1.88)
Endometrium (Friberg et al. 2007)	13 case–control studies	2.22	(1.80–2.74)
	3 cohort studies	1.62	(1.21–2.16)
Colon–rectum (Larsson et al. 2005)	6 case–control studies	1.36	(1.23–1.50)
	9 cohort studies	1.29	(1.16–1.43)
Bladder (Larsson et al. 2006)	7 case–control studies	1.37	(1.04–1.80)
	3 cohort studies	1.43	(1.18–1.74)
Non-Hodgkin's lymphoma (Mitri et al. 2008)	5 cohort studies	1.41	(1.07–1.88)
	11 case–control studies	1.12	(0.95–1.31)
Breast (Larsson et al. 2007)	5 case–control studies	1.18	(1.05–1.32)
	15 cohort studies	1.20	(1.11–1.30)
Prostate (Kasper & Giovannucci 2006)	9 case–control studies	0.89	(0.72–1.11)
	10 cohort studies	0.81	(0.71–0.92)

[a]Data on kidney cancer were not obtained from meta-analysis.

distributed to the liver (first passage insulin) where a relevant aliquot (up to 80%) is retained and degraded. The remaining hormone reaches the peripheral tissues through the systemic circulation. The liver/peripheral tissue insulin concentration ratio, therefore, ranges from 3:1 up to 9:1 during insulin secretion bursts. Exogenously administered insulin, in contrast, will arrive to peripheral tissues and to the liver at the same time and at a similar concentration. Peripheral tissue hyperinsulinemia due to exogenous insulin (circulating levels may peak two- to fivefold higher than normal endogenous levels, depending on the dose injected and the type of insulin or analog used) and the ensuing relative liver hypoinsulinemia, therefore, are a common condition in type 1 diabetic patients.

On the contrary, in most type 2 diabetic patients, hyperglycemia is associated with endogenous hyper-insulinemia, a compensatory state caused by insulin resistance. This condition often persists for many years (decades when including the pre-diabetes period before clinically evident diabetes is diagnosed). Hence, in these patients, the liver/peripheral tissue insulin concentration ratio reflects that of nondiabetic patients, but at a higher level. However, in contrast to normal individuals, in these diabetic patients, increased insulin secretion fails to replete body fuel storages in response to feeding because of insulin resistance. Therefore, in these patients, excess unused substrates (i.e. glucose) are present concomitantly with hyperinsulinemia. This abnormal situation is accompanied by a series of other abnormalities involving other hormones like glucagon, incretins, leptin, etc.

As DM persists for many years, this scenario is often subject to changes, with most type 2 diabetic patients progressively presenting decreased insulin secretion following the failure of b-cells, due to increased apoptosis rates that are not balanced by neogenesis. At this stage, patients with type 2 diabetes may become similar to type 1 diabetic individuals, with endogenous hypoinsulinemia and exogenous insulin requirement.

When studying type 2 diabetic patients, therefore, diabetes duration and insulin requirement may affect tissue exposure to insulin in different ways. If hyperinsulinemia has a role in promoting cancer initiation and/or progression, these aspects should be considered when determining the individual risk of a diabetic patient to develop cancer. Most studies on the diabetes–cancer association overlooked these different biological conditions.

In conclusion, diabetes is generally characterized by hyperglycemia and hyperinsulinemia, often coupled with a reduced metabolic effect of insulin (insulin resistance) in peripheral tissues. Chronic hyperinsuli-nemia, however, is a possible factor favoring cancer initiation and/or progression in diabetic patients due to the mitogenic effect of insulin. The heterogeneity and complexity of different tissue exposure to hyperinsulinemia in diabetic individuals does not allow the quantification of the role of insulin in promoting cancer risk in the different organs of different diabetic patients.

There are multiple and complex mechanisms poten-tially responsible for the mitogenic effects of insulin.

First, when insulin levels increase (as in the post-prandial surge in insulin-resistant subjects or after insulin injection), insulin may bind and activate the related insulin-like growth factor-I (IGF-I) receptor, which shares w80% homology with the insulin receptor (IR), but has a more potent mitogenic and transforming activity. Moreover, insulin decreases IGF-I-binding proteins (IGF-BP1 and, perhaps, IGF-BP2): this will result in increased free IGF-I, the biologically active form of the growth factor.

Secondly, many cancer cells have an increased IR content. The IR may be expressed in two different isoforms, A and B, produced by an alternative splicing of the IR gene transcript. In malignant cells, the A isoform (IR-A) expression is predominant, and its activation, at variance with the IR-B isoform, elicits more mitogenic than metabolic effects. By binding to the overexpressed IR-A, insulin may favor cancer progression and facilitate the growth of tumors that would otherwise have likely remained clinically irrelevant for an undetermined length of time.

Finally, insulin mitogenic activity might be enhanced at the cellular level by post-receptor molecular mechanisms, including insulin (or its synthetic analogs) residence time on the receptor and the intracellular up-regulation of the insulin mitogenic pathway. Experimental data indicate that this pathway, unlike the insulin metabolic pathway, may not be blunted in the condition of insulin resistance typical of diabetes (Fig. 4). The AMP-activated protein kinase (AMPK), mammalian target of rapamycin (mTOR), and insulin-signaling pathway represent three interrelated components of a complex mechanism controlling cell responses to nutrient availability, and their dysregulation may favor malignant cell proliferation in response to hyperinsulinemia.

In conclusion, strong but circumstantial evidence indicates a role for endogenous hyperinsulinemia and of exogenous insulin or analogs in promoting cancer growth in diabetic patients. However, the clinical relevance of this pro-cancer effect of insulin in diabetic patients is still unclear.

Anti-diabetic drugs that may influence cancer risk in diabetic patients

Most diabetic patients are treated for years or decades with a variety of drugs. The potential role of these drugs in favoring cancer is unclear but most likely minor, if any. Data are not conclusive because the large majority of diabetic patients change the drug dosage and/or the type many times during the course of the disease. Moreover, many are treated with more than one drug. Epidemiological studies on this issue, therefore, are difficult to interpret and often inconclusive.

The three major oral anti-diabetic drug families (sulphonylureas, biguanides, and thiazolidinediones) have a different mechanism of action. Sulphonylureas stimulate endogenous insulin secretion, while the other two categories of compounds are insulin sensitizers, i.e. they make tissues more responsive to insulin and, therefore, decrease hyperinsulinemia. If hyperinsuli-nemia plays a role in increasing cancer risk and progression in diabetic patients, it is reasonable to expect that these drugs will have a different effect on the association between diabetes and cancer. The biguanide metformin, widely used for more than 30 years and currently suggested as first-line therapy in type 2 diabetic patients, has been recently reported to reduce cancer risk when compared with untreated patients. In addition to lowering the amount of circulating insulin, another possible mechanism for the anti-cancer effect of metformin is the stimulation of AMPK (an enzyme inducing glucose uptake by muscles) and its upstream regulator LKB1, a well-recognized tumor suppressor protein. AMPK activators act as anti-proliferative agents because they reduce insulin (and IGF-I)-signaling downstream of the receptor and, therefore, inhibit insulin-stimulated proliferation. Hence, the anti-cancer effect of metformin can be explained by this dual mechanism.

Recent studies in MCF-7, BT-474, and SKBR-3 human breast cancer cells showed that in vitro metformin inhibited cell proliferation, reduced colony formation, and caused partial cell cycle arrest. These effects mainly occurred via MAPK, AKT, and mTOR inhibition and were replicated also in erbB2-overexpressing cells. On the basis of both epidemiological data and in vitro studies, a clinical trial for evaluating metformin activity on breast cancer cell proliferation (Ki67 index) is currently undergoing in 100 breast cancer patients.

Data on the other insulin-sensitizing drug (thiazoli-dinediones) are more controversial. A beneficial, neutral, or even deleterious effect has been reported for different types of cancer. The biological mechanism of these compounds is to activate PPARg receptors, which, in several in vitro experimental models, has shown a potential anti-cancer effect. In addition to lowering hyperinsulinemia, this effect can explain the described anti-cancer effect of glitazones. In any case, the use of these compounds is too recent and too limited to consider the present meager epidemiologic observations reliable.

The third group of drugs (sulphonylureas) are secretagogues, i.e. increase insulin secretion and cause hyperinsulinemia. As expected, therefore, they have been associated with an increased risk of cancer. Different sulphonylureas may have different effects, with glyburide being more deleterious than gliclazide. Although their effect on cancer risk is attributed to the prolonged hyperinsulinemia that they induce in patients, a direct effect on cancer (either positive or negative) cannot be excluded. Other factors that may influence the risk of cancer in diabetes are obesity, hyperglycemia, free fatty acids, chronic inflammation and oxidative stress.

THIAZOLIDINEDIONES AS ANTI-CANCER AGENTS[30]

I. TZDs and lung cancer

Although clinical data supporting the efficacy of TZDs in lung cancer is limited, *in vitro* studies as well as reports in experimental animals support this concept. *In vitro* studies available supporting the efficacy of TZDs in lung cancer are numerous. For example, the proliferation of A549 lung cancer cells was significantly inhibited by ciglitazone in a dose- and time-dependent manner both *in vivo* and *in vitro*, and PPAR-γ expression was markedly upregulated by ciglitazone treatment. Troglitazone induced PPAR-γ expression and apoptosis in two human lung cancer cell lines, but not in normal cells. These results suggest the potential for TZDs to target malignant cells without affecting normal cells (the goal of anti-cancer chemotherapy). In nude mice, direct injection of ciglitazone into A549-induced tumors suppressed the rate of tumor growth by 36%

While the modest anti-neoplastic effects of TZDs may preclude their use as monotherapy for treatment of lung cancer, combining TZDs with other anti-neoplastic agents could potentially enhance therapeutic efficacy. For example, the inhibitory effect of rosiglitazone on NSCLC cell growth was enhanced by the mammalian target of rapamycin (mTOR) inhibitor, rapamycin. mTOR is a serine/threonine kinase that is activated by Akt and regulates protein synthesis, and rapamycin has been shown to inhibit cell growth by blocking the action of mTOR. In addition to the above study, rosiglitazone potentiated gefitinib's anti-proliferative effects by increasing the expression of the tumor

suppressor, apoptotic gene, phosphatase and tensin homolog (PTEN). The combination of the low-dose apoptosis inhibitor, MK886, ciglitazone, and 13-cis-retinoic acid, produced synergistic growth inhibition of lung cancer cells (A549 and H1299) suggesting that targeting PPAR-γ and retinoic acid action could be a promising approach to suppress lung cancer growth. *In vitro* synergistic anti-proliferative and apoptotic effects were also observed by combining a novel TZD with imatinib in various malignant cell lines. The opportunities to optimize anti-cancer efficacy with various chemotherapy permutations involving TZDs are numerous and suggest their potential benefit. Further, the experimental efficacy of low doses of these agents in these studies suggests potential clinical efficacy with reduced toxic side effects, a major concern in cancer chemotherapy.

II. TZDs and breast cancer

PPAR-γ is expressed in normal and malignant mammary epithelial cells, and TZDs suppress breast carcinoma proliferation *in vitro* and in experimental animal models. Recently, PPAR-γ activation by conjugated linoleic acid was shown to have an anti-proliferative effect in MCF7 breast cancer cells. Breast cancer cells, along with prostate cancer and melanoma cells were shown to undergo apoptosis with PPAR-γ ligands was shown to induce differentiation of malignant breast epithelial cells. Interestingly, PPAR-γ acts as a tumor suppressor not only in breast, but also in skin and ovarian cancers. However, PPAR-γ was also shown to act as a tumor promoter in breast carcinogenesis. This seemingly paradoxical outcome was proposed either to occur after a cancer initiation event had already progressed, or to possibly occur following PPAR-γ-mediated activation of a cytokine or growth factor such as TGF-β, which depending on the stage of breast cancer, can either be tumor suppressing or tumor promoting. Nevertheless, the preponderance of evidence among studies examining TZDs in breast cancer cells suggests that PPAR-γ ligands inhibit proliferation and induce apoptosis both *in vitro* and *in vivo*. In addition, PPAR-γ ligands have been demonstrated to inhibit tumor angiogenesis and invasion in breast cancer. Particularly relevant information is expected to come from human studies. In patient tissue samples, PPAR-γ immunoreactivity was significantly associated with improved clinical outcome in breast carcinoma patients by univariate analysis. In addition, a recent pilot trial examined short-term (2−6 weeks) treatment with rosiglitazone in 38 women with early-stage breast cancer. Rosiglitazone (8 mg/d), administered between the time of diagnostic biopsy and definitive surgery did not elicit significant effects on breast tumor cell proliferation analyzed as expression of Ki67, a marker of tumor growth and progression as well as proliferation. In pretreatment tumors notable for nuclear expression of PPAR-γ as determined by immunohistochemistry, down-regulation of nuclear PPAR-γ expression occurred following rosiglitazone administration, contrary to what is expected. This TZD regimen was well tolerated and without serious adverse events. A prior trial reported in 2003 suggested that in patients with metastatic breast cancer, troglitizone failed to show any clinical benefits. Overall, clinical studies are not encouraging. Nevertheless, more and longer term clinical studies are warranted to determine if the promising results obtained in pre-clinical and *in-vitro* studies can be extrapolated to humans.

III. TZDs and colon cancer

In colon cancer, TZDs may also be of benefit. PPAR-γ mRNA and protein expression has been demonstrated in HT-29 colon cancer cells by RT-PCR and western blots, respectively, and PPAR-γ activation was associated with inhibition of cell growth through induction of apoptosis and suppression of the cell cycle. Similarly both the synthetic TZD, pioglitazone, and the natural ligand, 15d-PGJ_2, inhibited the proliferation of colon cancer cell lines in a dose-dependent manner that was reversed by the TZD antagonist GW9662.

IV.TZD mechanism of action in neoplasia

A. Apoptosis

One of the main mechanisms of action by which TZDs act as anti-cancer agents involves the induction of apoptosis, an effect that complements the growth suppressive properties of TZDs. A schematic representation of these effects is shown in Fig. 5.

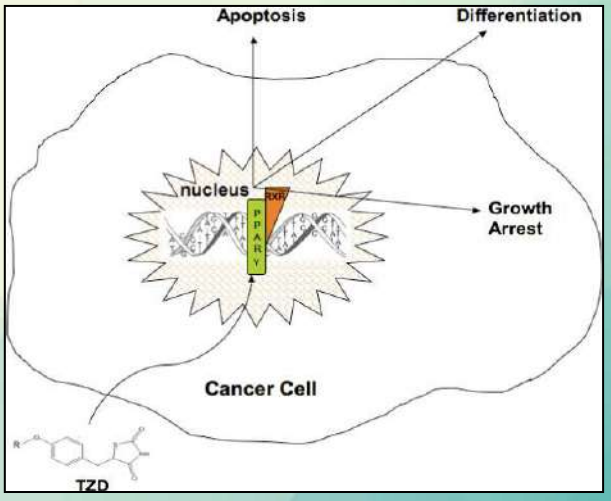

Figure 4. Activation of PPAR-γ by TZDs causes apoptosis, growth arrest, and differentiation in the cancer cell

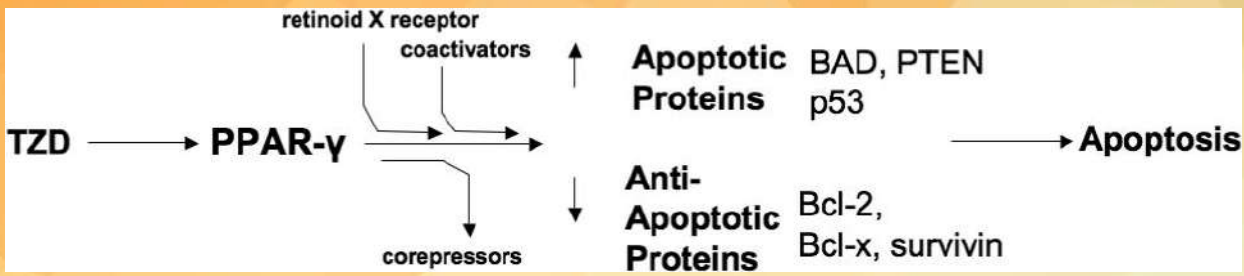

Figure 2. Mechanisms of TZD-induced apoptosis
TZDs activate PPAR-γ, stimulating heterodimerization with the retinoid X receptor, recruitment of coactivators, and the dissociation of corepressors which ultimately causes apoptosis by decreasing anti-apoptotic proteins such as bcl-2/bcl-x and survivin, while increasing the levels of the pro-apoptotic proteins, p53, bad and phosphatase and tensin homolog (PTEN).

Numerous studies support the notion that PPAR-γ activation induces apoptosis and thus exerts anti-cancer effects. For instance, in lung cancer cells troglitazone induced apoptotic activity that was PPAR-γ-and ERK1/2-dependent. Troglitazone treatment reduced the anti-apoptotic protein, bcl-2, and caused nuclear accumulation and co-localization of PPAR-γ and ERK. Similarly, treating colon cancer cells with rosiglitazone caused apoptosis, detected with TUNEL staining and flow cytometry. Although the exact mechanisms by which apoptosis was induced in that study were not defined, bcl-2/bcl- x (anti-apoptotic proteins), p53, bad (pro-apoptotic proteins), and the transcription factor NF-κB were implicated in PPAR-γ ligand-induced apoptosis. Rosiglitazone treatment also increased PTEN protein levels which can lead to apoptosis through the negative regulation of Akt. PTEN induction by PPAR ligands has also been reported to arrest tumor growth through PTEN's tumor suppressor effects.

B. Growth/cell cycle arrest

In addition to apoptosis, PPAR-γ activation may reduce tumor development through the arrest of cancer cell proliferation, through effects on cell cycle checkpoints or growth factor inhibition. One particularly well-known manner of suppressing proliferation rates involves cell cycle progression arrest. Cyclins are cell cycle regulators. Specifically, they are regulatory subunits of cell-cycle-specific kinases, and their activation is thought to regulate progress through the cell cycle. Cyclins are therefore potential oncogenes; and in fact, cyclin D1 overexpression and/or amplification are common features of several human cancers, thus promoting G1 phase progression. Exposure to TZD for 24 h caused G_0/G_1 cell cycle arrest. TZD treatment not only decreased protein levels of cyclin D1, but also reduced proliferating cell nuclear antigen, pRb, and Cdk4 and increased the cyclin-dependent kinase inhibitors p21 and p27, in a time-dependent manner (Yang et al, 2005b). Because the p21 and p27 kinase inhibitors inhibit CDK2/4 and CDK2 respectively, this can result in cell cycle arrest. In particular, increases in p21 expression levels have been attributed to Sp1 transcriptional activation (Han et al, 2004), as PPAR-γ has been shown to interact directly with transcription factors including Sp1 (Krey et al, 1995). In addition to p21, p18 was also demonstrated to be regulated by PPAR-γ (Morrison and Farmer, 1999). A schematic representation of some of these events is shown in Figure 6.

C. Differentiation

Another mechanism by which PPAR-γ activation may exert anti-neoplastic effects is through the promotion of cellular differentiation, and early as well as recent evidence indicates that TZDs might have favorable effects in the treatment of a variety of tumors as differentiation-inducing agents. PPAR-γ was demonstrated to induce differentiation in solid tumors both *in vitro* and *in vivo*. For example, TZD-induced differentiation of human cancer cells, defined as a shift toward a more steroidogenic phenotype, was mediated through activation of PPAR-γ-dependent pathways. TZD treatment in pancreatic cancer cells significantly inhibited growth through PPAR-dependent induction of pancreatic ductal differentiation without any increase in apoptosis. In HT-29 colorectal cancer cells, TZD treatment inhibited growth and metastasis through differentiation-promoting effects. In cultured breast cancer cells, PPAR-γ ligands caused extensive lipid accumulation and changes in epithelial gene expression associated with a more differentiated, less malignant state. In lung cancer cells, ciglitazone induced differentiation, and PPAR-γ expression inhibited tumorigenesis by reversing the undifferentiated phenotype of metastatic non-small-cell lung cancer cells and activating pathways that promoted a more differentiated epithelial phenotype.

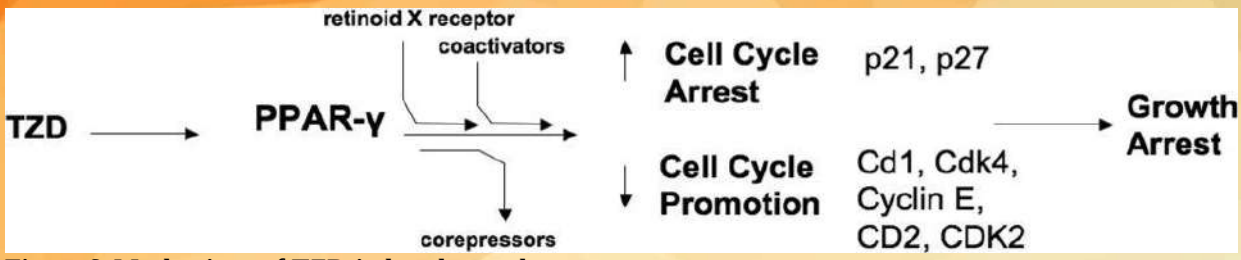

Figure 6. Mechanisms of TZD-induced growth arrest

In addition to apoptosis, PPAR-γ activation may reduce tumor development through the arrest of cancer cell proliferation and effects on cell cycle checkpoints. TZD treatment activates PPAR-γ, stimulating heterodimerization with the retinoid X receptor, recruitment of coactivators, and the dissociation of corepressors resulting in decreased protein levels of activated cyclins that regulate progress through the cell cycle. These include: cyclin D1 (Cd1), as well as Cdk4, Cyclin E, CD2, and CDK2. Conversely, TZDs increase the cyclin-dependent kinase inhibitors p21 and p27 that can inhibit CDK2/4 and CDK2 respectively, ultimately causing cell cycle arrest.

D. Additional considerations

The evaluation of other PPAR isoforms may also prove to be valuable in order to clarify the effect of PPARs on cellular differentiation. PPAR-β increased colonocyte differentiation as well as apoptosis in ligand-treated PPAR-β +/+ mice, whereas these effects were not found in PPAR-β −/− mice. Further, PPAR-β and PPAR-γ agonists altered mammary tumorigenesis and produced distinctive histopathologic patterns of tumor differentiation and development. Consistent with isoform-specific effects of PPARs, the specific TZD or PPAR ligand used may be of significant importance as differentiation effects seen with one ligand may not be observed in another. Clay et al, for example, reported that treating cells with $15dPGJ_2$ did not increase cellular differentiation, as had been seen in other neoplastic cells, but rather induced cellular events associated with programmed cell death or apoptosis.

V. PPAR-γ-independent mechanisms of tumor suppression

In addition to PPAR-γ-dependent actions, TZDs demonstrate a number of important PPAR-γ-independent effects. TZDs have been shown to stimulate the proteosomal degradation of cyclins D1 and D3, to block the G(1)-S transition through translation initiation inhibition, and to scavenge toxic reactive oxygen species (ROS) through PPAR-γ-independent mechanisms. Additional PPAR-γ-independent actions of TZDs include the induction of cellular acidosis through inhibition of the Na^+/H^+ exchanger, calcium storage depletion, and release of apoptotic factors from the mitochondria through the production of ROS. Other cited mechanisms by which TZDs exert anti-tumor effects in a PPAR-γ-independent manner include upregulation of PTEN/AMPK and down regulation of Akt/mTOR/p70S6 signaling cascades.

CONCLUSION

The complexity of the various diabetic conditions, the diversities in the biology of different forms of cancer, and the multiplicity of the possible mechanisms involved prevent a comprehensive and definite answer to many questions regarding the association of diabetes with an increased risk of cancer initiation and progression.

The available evidence indicates that the level of cancer risk related to diabetes will probably differ for each diabetic patient, on the basis of the cancer type and many other diabetes-related factors. Our present knowledge provides good evidence for a mild increase of cancer risk (and cancer mortality) in diabetic patients, more evident for some site-specific cancers. Present evidence, however, does not allow us to accurately define the general and the specific organ cancer risks in the individual diabetic patient. Because of the growing worldwide frequency of diabetes, this question needs to be properly addressed, in order to acquire a more rational approach to cancer prevention and treatment in diabetic patients.

A rapidly expanding body of literature has examined the ability of PPAR-γ-activating TZD ligands to contribute to cancer therapy as evidenced by numerous *in vitro* and *in vivo* studies. The results of these studies, while mixed, have fostered sufficient interest to stimulate the investigation of TZDs in clinical trials. Additional studies of PPAR-γ ligands in combination with other agents or in chemopreventive strategies merit further consideration. Whether the results obtained from *in vitro* and preclinical studies investigating the anti-cancer potential of PPAR-γ ligands will extrapolate to efficacy in human trials, remains to be determined. Clinical trials of adequate power and duration are required to clarify the role that PPAR-γ activation may have in the treatment of cancer.

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