Mesoporous Silica Nanoparticles for oil absorption

An Anti-obesity Nanotechnology

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Orlistat, an anti-obesity drug, is a lipase inhibitor can reduce fat absorption

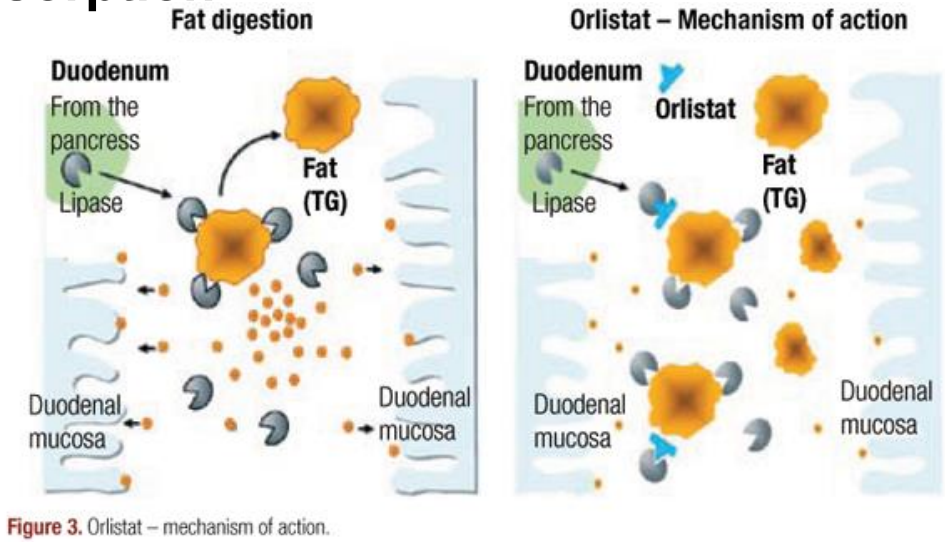
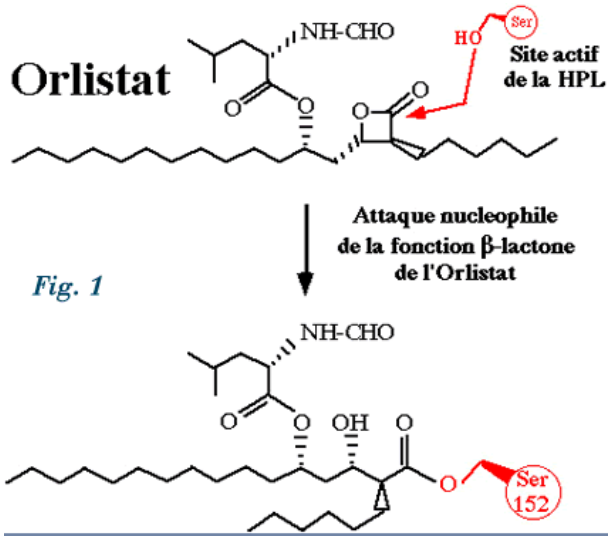


Figure 3. Orlistat – mechanism of action.



■ *Side effect*

http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-27302009000200018

Percentage of patients have side effects at first year

Side effect	XENICAL* % of Patients (N=1913)	Placebo* % of Patients (N=1466)
Oily Spotting	26.6	1.3
Flatus with Discharge	23.9	1.4
Fecal Urgency	22.1	6.7
Fatty/Oily Stool	20.0	2.9
Oily Evacuation	11.9	0.8
Increased Defecation	10.8	4.1
Fecal Incontinence	7.7	0.9

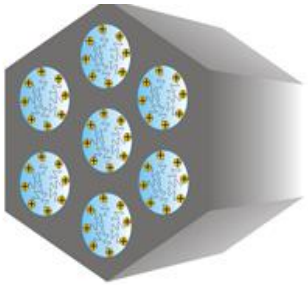
- ***Table taken from Xenical Package Insert Roche Pharmaceuticals***
- ***Treatment designates XENICAL 120 mg three times a day plus diet or placebo plus diet***

Invention Motivation: **The market of anti-obesity drug has been limited by uncontrollable side effects, such as Steatorrhea.**

Mesoporous silica nanoparticles (MSNs) as a oil curing agent

anti-obesity drug(Orlistat)

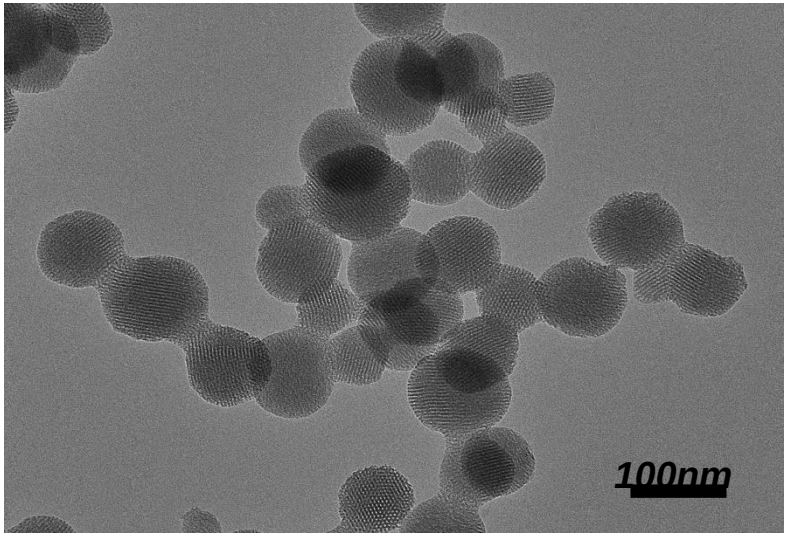
Reduce the side effect (steatorrhea, oily, loose stools)



In vitro Experiment

Material Characteristics:

Mesoporous silica NPs



TEM size:
102.1 ±16.17nm
DLS:132.8 ±30.24nm

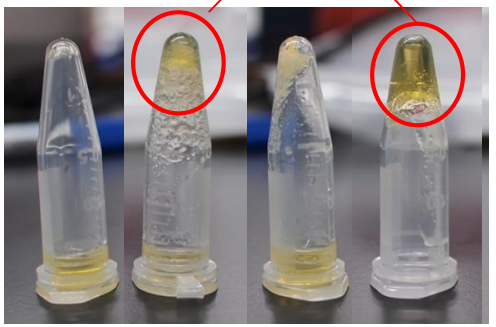
Surface area:1027.5m^3/g
Pore size: 2.56nm

Tube test:

curing phenomena

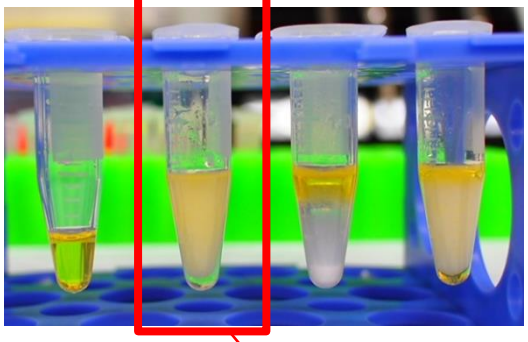
oil MSN SiO_2 MSN-TA

Without water



oil MSN SiO_2 MSN-TA

With water (pH=7.4)



MSN: mesoporous silica nanoaprticle
TA: tert-amino group

Most uniform

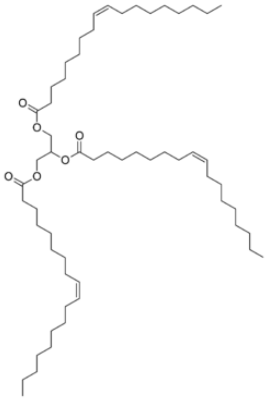
In vivo Efficacy

	Oil + orlistat	Oil + orlistat+ MSN	Oil + orlistat + MSN-TA	Oil + orlistat+ SiO_2
Dose	Oil:450mg Orlistat:25mg/ 1mL water	Oil:450mg Orlistat:25mg/ 1mL water MSN:60mg/ml	Oil:450mg Orlistat:25mg/ 1mL water MSN-TA:60mg/ml	Oil:450mg Orlistat:25mg/ 1mL water SiO_2:60mg/ml
Method	Oral	Oral (Orlistat and MSN mixture)	Oral (Orlistat and MSN-TA mixture)	Oral (Orlistat and SiO_2 mixture)
Efficacy (Eliminate ratio of Side Effect) Time: 24hr	0% (n=0/6)	**100% (8/8)**	17% (1/6)	0% (0/6)

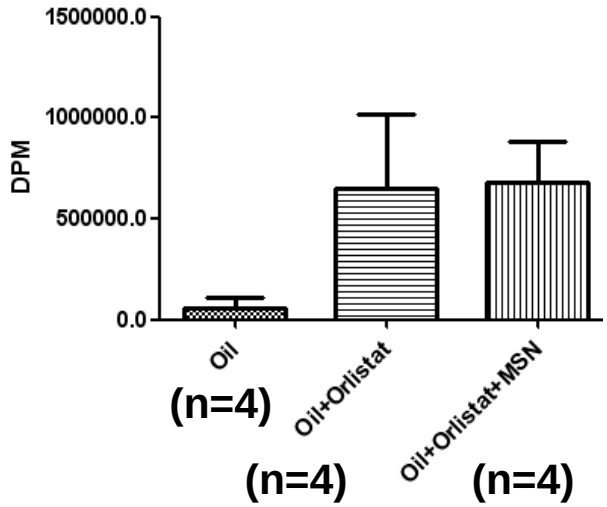
	Oil + orlistat	Oil + orlistat+ MSN	Oil + orlistat+ MSN	Oil + orlistat+ MSN
Dose	Oil:450mg Orlistat:25mg/ 1mL water	Oil:450mg Orlistat:25mg/ 1mL water MSN:60mg/ml	Oil:450mg Orlistat:25mg/ 1mL water MSN:40mg/ml	Oil:450mg Orlistat:25mg/ 1mL water MSN:20mg/ml
Method	Oral	Oral (Orlistat and MSN mixture)	Oral (Orlistat and MSN mixture)	Oral (Orlistat and MSN mixture)
Efficacy (Eliminate ratio of Side Effect) Time: 24hr	0% (n=0/6)	**100%** **(8/8)**	25% (1/4)	0% (0/4)

Process: Using Isotope labeled oil to prove the MSNs does not affect the function of orlistat

Oliver Oil labeled with H^3-triolein

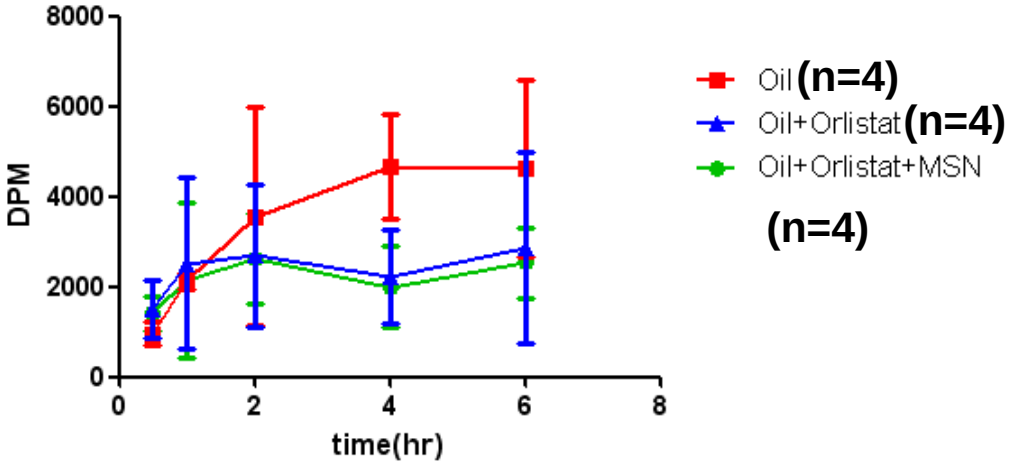


H^3-triolein in feces(24hr)



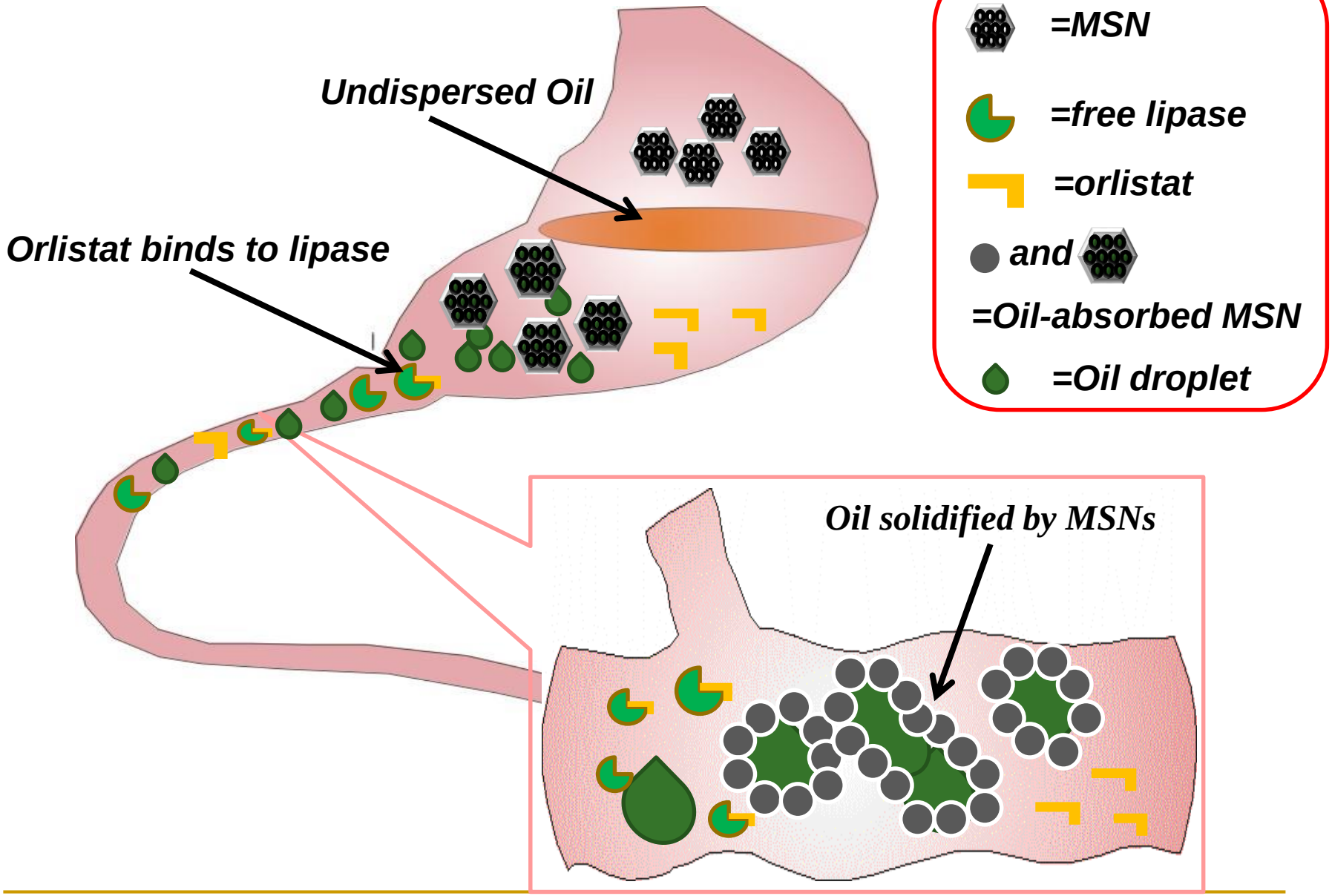
(n=4) (n=4) (n=4)

H^3-triolein in blood



MSN doesn't affect the function of orlistat

Mechanism Hypothesis



Comparison with *Prior* Arts

	CNMR Invention: MSN Materials (Mesoporous silica nanoparticles)	Prior Art 1: Gastrointestinal side effects of orlistat may be prevented by concomitant prescription of natural fiber (ref: International Journal of Obesity(2001),25, 1095~1099)	Prior Art2: Method of reducing gastrointestinal side effect associated with orlistat treatment (ref: US 6756364 B2)
Components	SiO_2	**Psyllium mucilloid** Plant fiber	Cholestyramine, colestipol, Diethylaminoethylcellulose Starch derivatives
Dosage	Orlistat(25mg): MSN(60mg)= **1:2.4**(rat)	Orlistat(120mg): Psyllium mucilloid(6g) =**1:50**(human)	Orlistat(120mg) Cholestyramine, Colestipol:4000mg Diethylaminoethylcellulose:240mg Starch derivatives: 740mg
Drug Ratio (Orlistat : additive materials)	**1:18.5**	**1:50**	**1:42**
Side effect		**High dose: the risk of bowel obstruction**	Colestipol can induce **Gastrointestinal disturbances, especially (mild, occasionally severe) constipation**

- **Patent Name:** MESOPOROUS SILICA NANOPARTICLES FOR OIL ABSORPTION
- **Patents Granted & Issued:**

  US9185928 B2

  EP Granted on April. 11, 2017